VOLUME 79 NUMBER 1

AMERICAN JOURNAL

OF

DISEASES OF CHILDREN

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JANUARY 1950

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO 10, ILLINOIS. ANNUAL SUBSCRIPTION, $12.00

Entered as Second Class Matter Jan. 4, 1911, at the Postoffice at Chicago, Under the Act of Congress of March 3, 1879

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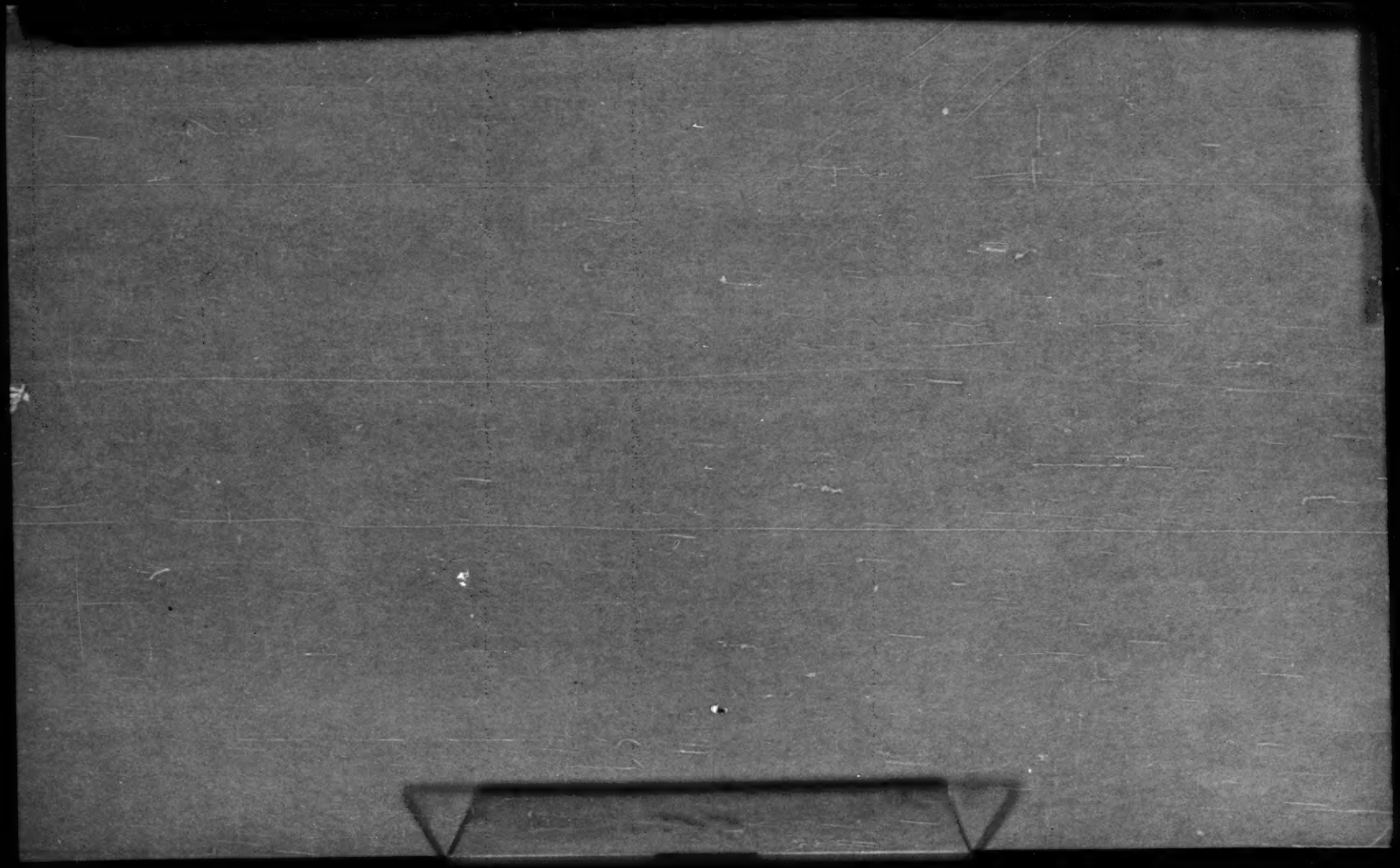

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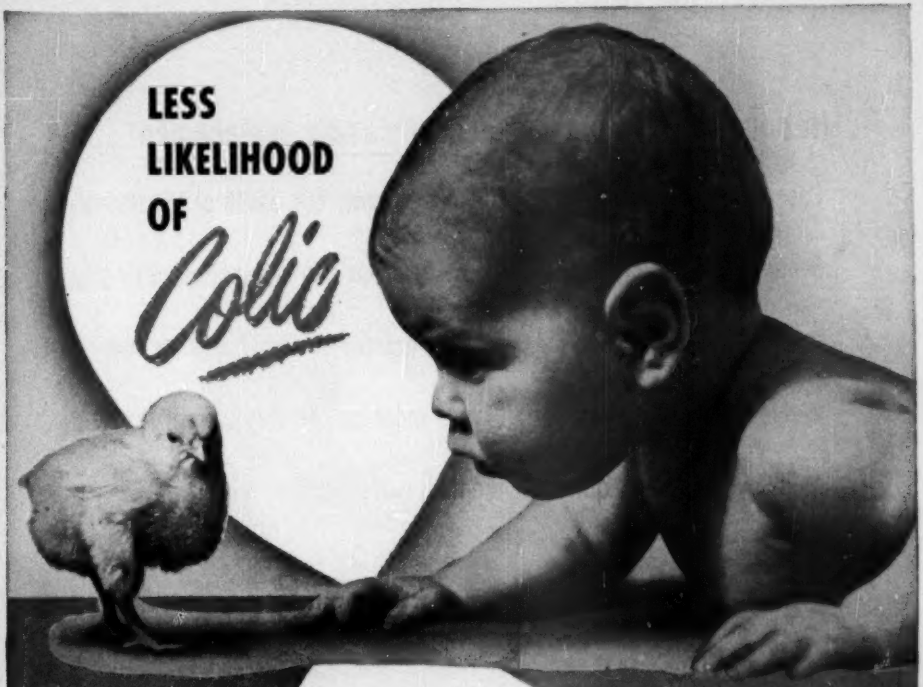

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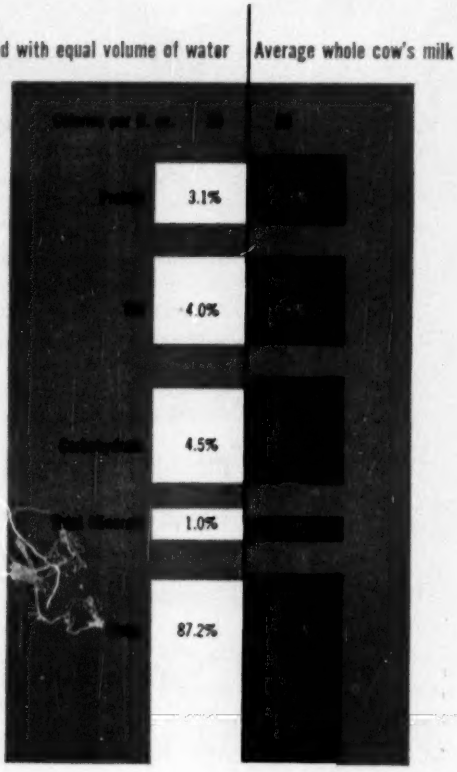

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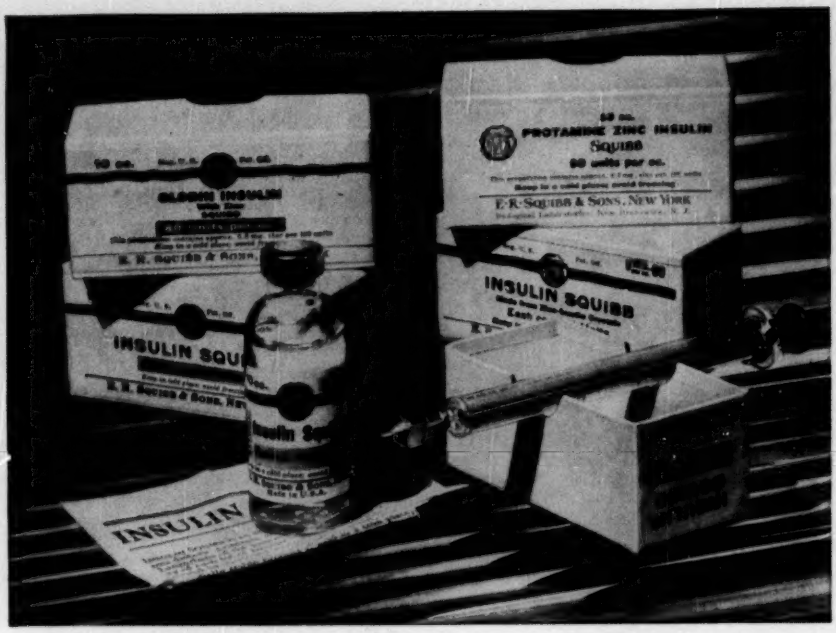

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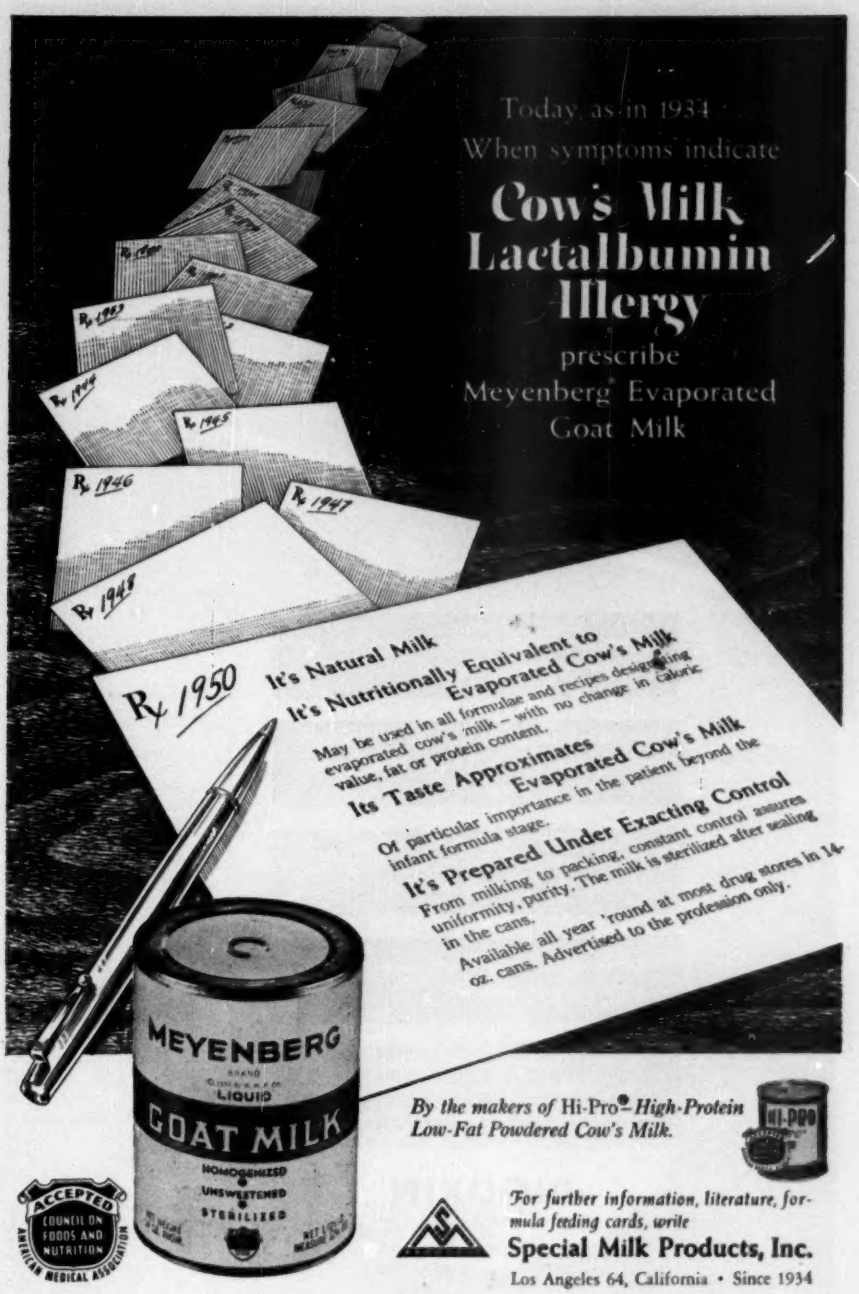
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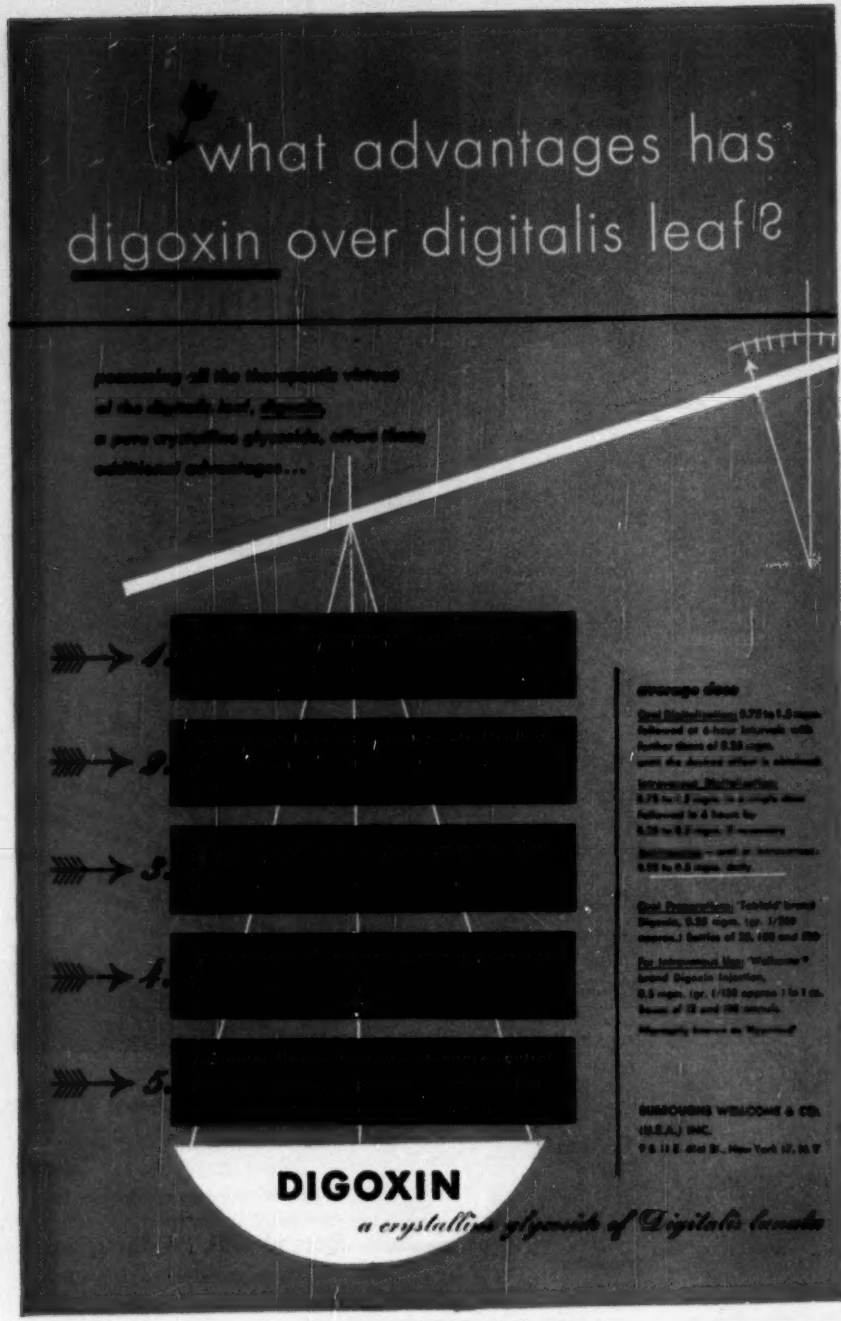
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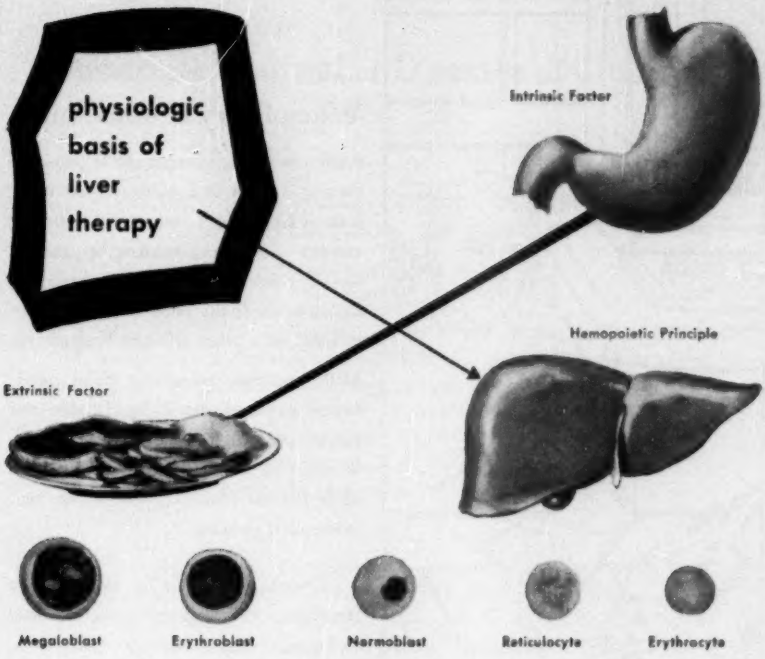

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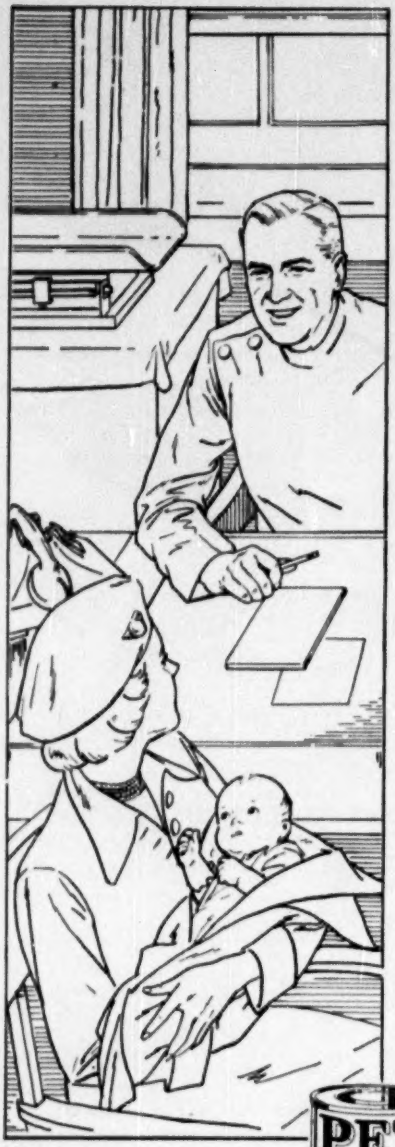

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PHYSIOLOGIC BACKGROUND OF FETAL ANOXIA AT BIRTH AND CYANOSIS IN THE NEWBORN

CLEMENT A. SMITH, M.D.
BOSTON

THE FACT that representatives of two specialties, obstetrics and pediatrics, are at this meeting indicates the interest of us all in every stage of the period that begins with an intrauterine fetus and ends with an extrauterine baby. Therefore, both the fetus and the newly born infant will be dealt with in this review of the fundamental principles of anoxia and cyanosis. In conclusion, an attempt will be made to describe briefly the beginning of extrauterine respiration.

ANOXIA

Although anoxia is the subject of a vast literature, the facts have not changed since Means in 1924 [1] clarified them by the diagrams presented, in somewhat modified form, in figure 1. It will be noted from the scheme of each diagram that in passage through the capillaries blood gives up a certain amount of its oxygen and simultaneously undergoes a decline in its oxygen tension. The amount of oxygen is expressed as volumes per cent, or the cubic centimeters of oxygen deposited in the tissues of each 100 cc. of blood traversing them. Oxygen tension may (loosely) be thought of as the head of pressure under which this gas is delivered. The measurement of this, in millimeters of mercury, is just as factual as is that of the amount of oxygen in the blood. However, whereas any given amount of oxygen is the same whatever the pressure at which it is carried, this element of pressure or tension makes a real difference in the delivery of that amount to the cells themselves.

The term "anoxic anoxia" seems a cumbersome tautology, but it has real meaning as signifying that the prime fault is with the oxygen available to the blood rather than with the transporting apparatus. The

From the Laboratory for Research on the Newborn, Boston Lying-in Hospital, the Children's and Infants' Hospitals and the Department of Pediatrics, Harvard Medical School.

Introductory paper of a panel discussion on fetal anoxia at birth and cyanosis of the newborn presented at the joint meeting of the Section on Pediatrics and the Section on Obstetrics and Gynecology at the Ninety-Seventh Annual Session of the American Medical Association, Chicago, June 25, 1948.

1. Means, J. H.: Dyspnea, Medicine **3**:309-416 (Aug.) 1924.

diagrams are drawn to show that in passage from arteries to veins, whether normally (upper diagram), or in anoxic anoxia (lower left) or in anemic anoxia (lower right), each 100 cc. of blood gives up about 5 cc. of oxygen, an amount which is somewhere near the usual arteriovenous difference at rest. But inspection of the oxygen tensions under which this transaction takes place clearly shows that in the anoxic form the pressure is subnormal at the arterial end and necessarily still lower at the venous end of the unloading range. On the other hand, in anemic anoxia the tension is below normal at the venous end only, having fallen too precipitately as the capillaries are traversed. Stagnant

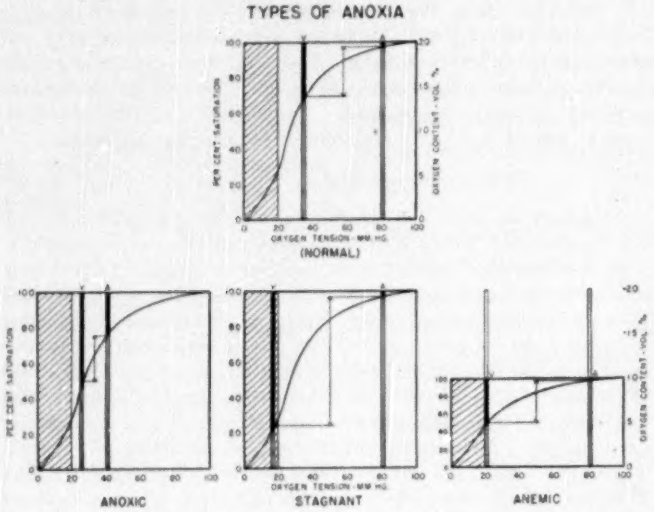

Fig. 1.—Oxygen saturations and tensions in arterial and venous blood in three varieties of anoxia (lower part) contrasted with the normal (upper part). Columns *A* and *V*, representing arterial and venous blood respectively, are diagonally shaded to indicate oxygenated hemoglobin and blackened to indicate reduced hemoglobin. The shaded area at the left roughly indicates the oxygen tension of the tissues. (Based on the original diagrams of Means [1] and reproduced, with alterations and by permission, from Best and Taylor.[2])

anoxia (lower middle) occurs because a sluggish flow, although allowing a greater than normal deposit of oxygen in terms of amount, nevertheless delivers it at a low tension at the venous end of the capillary. Thus, a poor gradient of pressure is provided to force the necessary oxygen into the tissue cells along much of the capillary bed. Although combinations of types, such as anoxic plus stagnant anoxia, can accentuate the effects of each individually, the anoxic form embodies

the greatest difficulties for the tissues, is thus of more serious import than the others and, therefore, will be discussed at greater length. Best and Taylor [2] offered a list of clinical mechanisms causing anoxic anoxia, which has been modified to suit present purposes:

1. Failure of central stimulation or regulation of breathing
2. Low oxygen tension in inspired air
3. Pulmonary disturbance: obstructed airway, atelectasis, pneumonia, pulmonary edema and emphysema
4. Unaerated right to left shunts through or around the heart

In all these situations the blood distributed by the large arteries is insufficiently saturated with oxygen. Let us look at this list first as it may apply to the fetus. Mechanism 1 will obviously not apply in fetal life, because the fetus does not get its oxygen by breathing but via the maternal circulation, placenta and cord. However, the fetus may be the ultimate victim of the second and third mechanisms on the list if the mother is breathing an anesthetic gas low in oyygen, such as one with a strong mixture of nitrous oxide,[3] or has any serious respiratory or circulatory disturbance. Moreover, because the placenta serves as a lung one may substitute, so far as the fetus is concerned, pathologic changes of the placenta and cord for the pulmonary disturbances comprising the third mechanism of the list. The fourth mechanism is scarcely applicable to the fetus, which, of course, normally exists by means of right to left circulatory shunts.

Once the fetus is born and is dependent on its own lungs (and, ultimately, on its respiratory centers), mechanism 1 becomes of fundamental importance. Anoxia will rapidly become total if there is no respiratory impulse. The newborn infant is unlikely to be exposed to reduced atmospheric oxygen tensions, but the pulmonary disturbances of mechanism 3 are characteristically frequent and were fully discussed in the other papers of this series (those by Eastman, Clifford and Zuelzer published in the December 1948 issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN, pp. 661 to 688). The circulatory abnormalities of mechanism 4 occur in numerous instances of congenital anomalies of the heart and great vessels.

Although anoxic anoxia, with its particularly serious implications, is the form most apt to occur in fetuses and newborn infants, it is fortunately the one most apt to be alleviated by the administration of oxygen. Unless due to complete failure of the nervous impulse, or

2. Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice, ed. 4, Baltimore, Williams & Wilkins Company, 1945.

3. Eastman, N. J.: Fetal Blood Studies: V. The Rôle of Anesthesia in the Production of Asphyxia Neonatorum, Am. J. Obst. & Gynec. **31**:563-572 (April) 1936.

to anatomic shunt, the fundamental discrepancy in saturation of arterial blood can be mitigated, if not completely removed, by elevation of the oxygen content of the inspired air. Since 100 cc. of air contains about 21 cc. of oxygen at a partial tension only one-fifth that of the atmosphere, it is possible by the addition of more oxygen to double, triple or even quadruple its amount and tension in the air reaching the lungs of the mother before birth or of the baby after birth. Even though diffusion into the blood continues to be impaired, a proportionate improvement will occur in the amount and tension of oxygen reaching the pulmonary circulation, and thence the left side of the heart and the aorta, the placenta, in the case of the fetus in utero, or the tissues, in the case of the newborn infant.

Stagnant anoxia in the fetus scarcely needs consideration, but, since slowing of the blood stream accompanies any condition of impaired circulation, stagnant anoxia occurs with great frequency in the extremities during the immediate newborn period. Local cooling introduces the further effect of reduced blood flow because of capillary constriction. The more generalized, prolonged and serious stagnations are those resulting from cardiac weakness and states akin to shock, which are often, in turn, the results of anoxic anoxia affecting the cardiac muscle and other tissues essential to circulation. Other vicious cycles will suggest themselves. Purely stagnant anoxia cannot be relieved by administration of oxygen, because the blood leaving the left side of the heart is already normally oxygenated.

Anemic anoxia can occur only rarely (from gross hemorrhage) to organisms so well supplied with hemoglobin as are fetuses and newborn infants. If, however, part of the normal quantity of hemoglobin is converted to methemoglobin, enough oxygen-carrying material is thus withdrawn from service that a form of anemic anoxia is the result. Instances of this sort, caused by poisoning from nitrites or certain dyes, have been reported with increasing frequency.[4] It is obvious from the diagram that anemic anoxia will not be altered by administration of oxygen.

CYANOSIS

Consideration of cyanosis, even briefly, requires an altered approach.[5] No matter how much total hemoglobin is present, and, indeed, whatever the amount of oxyhemoglobin, cyanosis will not be observed unless

4. Wallace, W. M.: Methemoglobinemia in an Infant as a Result of Bismuth Subnitrate, J. A. M. A. **133**:1280-1281 (April 26) 1947. Cornblath, M., and Hartmann, A. F.: Methemoglobinemia in Young Infants, J. Pediat. **33**:421-425 (Oct.) 1948. Graubarth, J.; Bloom, C. J.; Coleman, F. C., and Solomon, H. N.: Dye Poisoning in the Nursery, J. A. M. A. **128**:1155-1157 (Aug. 18) 1945.

5. Lundsgaard, C., and Van Slyke, D. D.: Cyanosis, Medicine **2**:1-76 (Feb.) 1923.

a certain amount of reduced hemoglobin is present in the capillaries. Therefore, I shall now cease considering oxygen amounts and tensions and turn to the subjects of oxygen unsaturation or reduced hemoglobin. Cyanosis occurs at any region of the body where each 100 cc. of capillary blood contains 5 or more grams of hemoglobin in reduced form. Since the amount of unsaturated hemoglobin is a simple fraction or percentage of the total amount of hemoglobin present, the more concentrated a person's blood is in hemoglobin the more readily will he become cyanotic. Newborn infants are, therefore, physiologically predisposed to cyanosis, as clinical experience will easily demonstrate.

A newborn subject with 20 Gm. of hemoglobin per hundred cubic centimeters would be cyanotic in circumstances which, were he 3

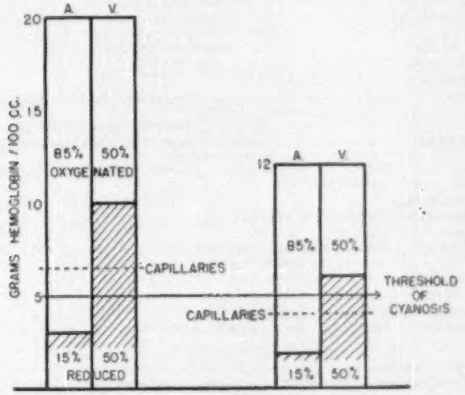

Fig. 2.—Graph showing relation between hemoglobin concentration and appearance of cyanosis. It illustrates that similar percentage saturations of arterial (*A*) and venous (*V*) blood will result in oxygen unsaturation of capillary blood above the threshold of cyanosis in an infant with 20 Gm. of hemoglobin per hundred cubic centimeters of blood (left) but will not produce cyanosis in an infant with 12 Gm. of hemoglobin per hundred cubic centimeters of blood (right).

months older and his hemoglobin concentration at 12 Gm. per hundred cubic centimeters, would produce no cyanosis, as is shown in figure 2. Moreover, if the infant at the latter stage were given a transfusion so that his hemoglobin concentration was raised to 20 Gm., he might then become cyanotic as an indirect result of the transfusion. Parenthetically, this artificially induced cyanosis would not signify a worse condition than that of the pretransfusion anemia without cyanosis. Without going into further details, I may say that it has been demonstrated that impaired oxygenation of blood in the lungs, considered previously as a major cause of anoxic anoxia has the most pronounced

effect of all the conditions tending to produce or augment cyanosis. Therefore, in the newborn infant, with both a relative polycythemia and a predisposition to anoxic anoxia, one has an organism likely on two counts to become cyanotic.

Cyanosis, not harmful per se though usually accompanying harmful circumstances, can be an extremely helpful guide to differential diagnosis. Thus, if merely increasing the amount of oxygen breathed by a cyanotic infant definitely improves his color, his cyanosis must have been related to anoxia from a respiratory disturbance originating at the central nervous system, in the airway or in the lungs themselves. The elevated oxygen concentration in the lungs proportionately raises

Relationship of Anoxia and Cyanosis

Type of Anoxia	Cause of Cyanosis
1. Anoxic anoxia (low tension throughout capillary bed)	
A. Fetal *:	Maternal pulmonary or circulatory disease; anesthetic gas replacing maternal oxygen Interference with placental exchange; obstructed cord
B. Neonatal;	Poor aeration of blood in lungs * from numerous central nervous system and pulmonary causes Right to left shunts † caused by cardiac or circulatory malformations
2. Stagnant anoxia (low tension at venous end of capillary bed)	
A. Fetal:	Unlikely
B. Neonatal †:	Cold; circulatory weakness, shock, effects of other forms of anoxia on heart
3. Anemic anoxia (rapid drop in tension)	
A. Fetal:	Extremely unlikely
B. Neonatal:	Occasional, from massive hemorrhage or methemoglobinemia †

* Production of cyanosis which may be improved by administration of oxygen.
† Production of cyanosis which is not improved by administration of oxygen.

that of the arterial and capillary blood and the amount of reduced hemoglobin is correspondingly decreased. On the other hand, if enrichment of oxygen in the respired air does not alter visible cyanosis, some other explanation must be advanced for the unsatisfactory skin color. The possibilities are then a right to left shunt, stagnation (from poor circulation, shock or local chilling) or, finally, the presence of an abnormally colored hemoglobin compound. To sort out all the elements of anoxia, cyanosis and the effects of oxygen administration, the accompanying generalized summary is presented in table form.

ONSET OF BREATHING AT BIRTH

Consideration of physiologic backgrounds for this discussion now requires a brief statement of present day beliefs regarding the onset of extrauterine respiration. These depend largely on the work of Barcroft.

who, in the last years of his life, arrived at an explanation of the way breathing begins at birth which fits the observed facts closely.[6]

Respiratory onset after delivery apparently may follow one of two patterns, each evoked by a different mechanism. A simple diagram (fig. 3) illustrates these two patterns. On the one hand is the desirable situation in which respiration begins at once after birth as a more or less rhythmic integration of inspiration followed by expiration, frequently punctuated or replaced by crying. Infants exhibiting this pattern are strikingly responsive to cutaneous and proprioceptive sensations. The experimental animal fetus, approached with great operative care in the opened uterus of its locally or spinally anesthetized mother, displays this same sensitivity to cutaneous stimulation and responds to stimuli in the same way—by rhythmic movements of the

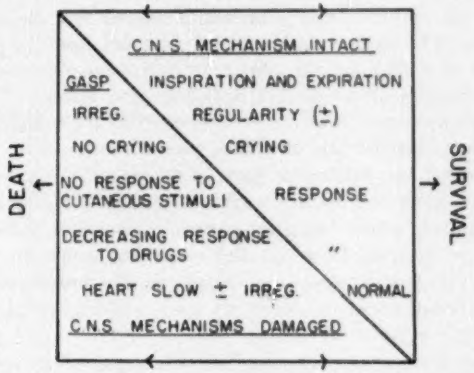

Fig. 3.—Pattern of respiratory onset in the infant with intact central nervous system (right) as contrasted with that in infant with impairment of the central nervous system, as from anesthesia, anoxia or trauma. Arrows at top and bottom of diagram indicate that the situation of any infant may move in either direction in the immediate postnatal period.

respiratory muscles. This integrated reflex from physical stimuli may be taken as the normal pattern of respiratory onset and the one exhibited by the undamaged, well oxygenated and nonnarcotized infant at birth.

At the other end of the scale are those infants whose respiratory onset, usually delayed, is a series of irregular gasps without a true expiratory component. These efforts are actually instantaneous inspira-

6. Barcroft, J.: (*a*) The Respiratory Function of the Blood: III. Transition from Placental to Pulmonary Respiration, J. Roy. Inst. Pub. Health & Hyg. **9**:86-95 (March) 1946; (*b*) Researches on Pre-Natal Life, Springfield, Ill., Charles C Thomas, Publisher, 1948.

tions, never accompanied with crying and—as clinical experience easily demonstrates—not to be produced by cutaneous stimuli and only decreasingly obtained in response to drugs. This type of respiratory onset can also be experimentally reproduced, as Barcroft demonstrated, in the fetus of a deeply anesthetized animal mother, by occluding the attached umbilical cord and waiting a minute or so until anoxia mounts to a certain critical height. The movement suggests the gasp produced by inhalation of hydrocyanic acid and represents an analogous phenomenon. It is the primitive, disintegrated response of an impaired central nervous system. Nevertheless, and especially if aided by an increased oxygen content of the surrounding air, these irregular gasps may "secure enough oxygen to bring the higher parts of the brain into action and a rhythm establishes itself . . . the dying foetus in its last effort [opens] the door to life and a free existence."[6a]

These two patterns may represent a regular and an emergency mechanism. The regular one seems to be a reflex from the peripheral stimulation of cooling and the other sensory changes of a new environment. It requires an unimpaired central nervous system. The emergency mechanism may often be in reserve when these higher centers are not functioning because of anoxia, hemorrhage or severe narcosis. It may depend in considerable part on the so-called chemoreceptors (the aortic and carotid bodies) until the improved oxygenation of the brain as a whole allows medullary centers to come into activity. Any action to be expected from so-called respiratory stimulants, such as lobeline, takes place on these chemoreceptors. The immediate response to lobeline, when it can be secured, is a series of intense gasps rather than a gentle, rhythmic breathing.[7]

Between the extremes of these patterns lies a whole spectrum of possible shadings. The clinician will find it helpful to study any newborn patient with regard to its place in that range of possibilities and to bend every effort to see that the infant's status moves toward the right side of the diagram rather than toward the left. The other papers of this panel referred to previously may enlighten him concerning what these efforts should be.

The physiologic basis for this discussion may be completed by a few more statements. It should be stressed that the original inflation of any alveolus requires more force from the infant—or from the physician in his behalf—than do the breaths which follow.[8] An intrapleural negative pressure of 25 to 30 cm. of water (and even more in

7. Schmidt, C. F.: Physiologic Phenomena Related to Anesthesia, Anesth. & Analg. **17**:24-34 (Jan.) 1938.

8. Wilson, J. L., and Farber, S.: Pathogenesis of Atelectasis of the Newborn, Am. J. Dis. Child. **46**:590-603 (Sept.) 1933.

certain abnormal circumstances) may be needed for the primary separation of moist alveolar surfaces, while 10 to 15 cm. of water pressure may be sufficient thereafter. Although forces of considerably more than 30 cm. of water pressure are inherent in the normal infant's thoracic apparatus, it is likely that such pressures cannot safely be long continued if the lung as a whole is not expanding and a few areas become overstretched. Fortunately, a surprising amount of oxygen appears to be absorbable from the bronchi and bronchioles and, even, from air swallowed into the stomach, and this may go far to support the infant while his alveoli gradually expand. Finally, should attempts based on the soundest physiologic principles fail to succeed, it must be borne in mind that an autopsy will sometimes uncover not the cause but only the effects of anoxia. If the cause is anatomic, the pathologist can be expected to find it. He cannot be expected to demonstrate purely pharmacologic or biochemical disturbances.

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PROTAMINE TETANUS TOXOID

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A NUMBER of reports dealing with reactions following immunization against tetanus have appeared in recent years.[1] The elimination of Witte's® peptone from the medium in which the bacillus is grown seemed to reduce the frequency of disturbing reactions. Nevertheless, it appears desirable to improve on the fluid toxoids being used, as well as on the product obtained by the simple addition of relatively large amounts of alum to such crude toxoids. Several methods of purifying crude toxoid or toxin have been described in the literature. Boivin and Izard[2] used trichloroacetic acid to precipitate the toxoid and thereby obtained a considerable removal of inert substances. Eaton and Gronau[3] precipitated tetanus toxin with cadmium chloride, after

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The part of this work which was carried out at Columbia University by one of us (V. R.) was supported by a research grant from the National Institute of Health and administered by Prof. Edgar G. Miller Jr., as well as by grants 551 and 581 from the Council on Pharmacy and Chemistry of the American Medical Association.

1. Cooke, R. A.; Hampton, S.; Sherman, W. B., and Stull, A.: Allergy Induced by Immunization with Tetanus Toxoid, J. A. M. A. **114**:1854 (May 11) 1940. Whittingham, H. E.: Anaphylaxis Following Administration of Tetanus Toxoid, Brit. M. J. **1**:292, 1940. Parish, H. J., and Oakley, C. L.: Anaphylaxis After Injection of Tetanus Toxoid, ibid. **1**:294, 1940. Cunningham, A. A.: Anaphylaxis After Injection of Tetanus Toxoid, ibid. **2**:522, 1940. Gold, H.: Sensitization Induced by Tetanus Toxoid Alum-Precipitated, J. Lab. & Clin. Med. **27**:26, 1941. Swartz, A.: Allergic Manifestations in Atopic Individuals Following Injection of Tetanus Toxoid, J. Allergy **14**:544, 1943.

2. Boivin, A., and Izard, Y.: Méthode pour la purification, à l'acide trichloracétique, des toxines et anatoxin, diphtériques, tétaniques et staphylococciques. Compt. rend. Soc. de biol. **124**:25, 1937.

3. Eaton, M. D., and Gronau, A.: Comparative Studies on Purification of Tetanus and Diphtheria Toxins, J. Bact. **36**:423, 1938.

a previous treatment with calcium chloride. Toxin was then eluted and reprecipitated with ammonium sulfate and the latter removed by dialysis. Pickett, Hoeprich and Germain,[4] following the same procedure and applying it to toxin prepared in the medium of Mueller and Miller,[5] obtained a toxin containing 2×10^{-6} mg. of nitrogen per mouse minimum lethal dose. Pillemer, Wittler and Grossberg [6] reported the isolation of crystalline toxin by means of several reprecipitations with methanol at low temperatures and controlled p_H and ionic strength. With a similar technic, they have prepared toxoid with about 600 Lf units [7] per milligram of nitrogen.[8]

Since we previously used protamine for the purification and precipitation of diphtheria toxoid,[9] it appeared probable that the same process could be followed in the case of tetanus toxoid. The present report describes a simple method for precipitating tetanus toxoid with this reagent and leaving behind a large proportion of the inert, nitrogen-containing protein derivatives used in preparing the broth. The results of nitrogen analyses of the precipitated toxoid and the antitoxin titers produced by guinea pigs, as well as by several children, given injections of the protamine toxoid are presented. The protamine-precipitated toxoid still contains protein, or proteins, capable of giving a precipitate when mixed with serum of rabbits given injections of dead tetanus bacilli washed free of toxin; one may refer to this protein as "bacillary protein" by analogy with the corresponding protein in the case of diphtheria bacillus. Nevertheless, a notable refinement is effected by a single step consisting of the addition of protamine, which precipitates the toxoid and leaves, in solution, 98 to 99 per cent of the nitrogen of the broth, most of which is derived from the proteose and peptone of the latter. The protamine-toxoid complex contains 500 to 650 Lf units per milligram of nitrogen (after deduction of nitrogen derived from protamine present).

4. Pickett, M. J.; Hoeprich, P. D., and Germain, R. O.: Purification of High Titer Tetanus Toxin, J. Bact. **49**:515, 1945.

5. Mueller, J. H., and Miller, P. A.: Production of Tetanal Toxin, J. Immunol. **50**:377, 1945.

6. Pillemer, J.; Wittler, R., and Grossberg, D. B.: The Isolation and Crystallization of Tetanal Toxin, Science **103**:615, 1946.

7. The Lf unit is that amount of toxoid (or toxin) which flocculates most rapidly with 1 unit of antitoxin in a series of mixtures containing constant amounts of toxoid (or toxin) and varying amounts of antitoxin.

8. Pillemer, L.; Grossberg, D. B., and Wittler, R. G.: The Immunochemistry of Toxins and Toxoids: II. Preparation and Immunological Evaluation of Purified Tetanal Toxoid, J. Immunol. **54**:213, 1946.

9. Ross, V.: Preparation and Immunizing Properties of Protamine Diphtheria Toxoid, Am. J. Dis. Child. **68**:172 (Sept.) 1944. Ross, V.; Clapp, F. L., and Schimpf, B. W.: Antitoxin Titers Following Immunization with Protamine-Precipitated Diphtheria Toxoid, Am. J. Pub. Health **36**:645, 1946.

METHOD

Toxin was produced by growing the tetanus bacillus in broth, the principal constituents of which were beef heart infusion, a peptic digest of beef heart and glucose.[10] There were 100,000 minimum lethal doses (for the guinea pig) per

TABLE 1.—*Antitoxin Titers of Guinea Pig Serums After One Injection of Protamine Tetanus Toxoid*

Experiment Number	Mg. of Protamine Added per Cc. of Fluid Toxoid	Mg. of Alum Added per Cc. of Fluid Toxoid	Lf Units per Cc. of Final Suspension	Volume of Injection, Cc.	Antitoxin (American Units) per Cc. of Pooled Serum, After	
					4 Weeks	6 Weeks
1a	1	0.4	10	1	1 to 2	8
b	2	0.4	10	1	1	4 to 6
c	3.5	0.4	10	1	<1	2
d	3.5*	0.4	10	1	2	7
2a	1	0.4	10†	1	2	5 to 6‡
b	1	1.6§	10†	1	<1	5 to 8‡
c	1	1.6§	10†	1	1 Slightly <1	4 to 6
3a	1	0.4	30	0.5	1	7
b	1	0.4	12	1 Slightly	<1	2 to 3
c	1	1.6	12	1	<1	2
4	1.25	0.4‖	10¶	1	1	1
5a	1	0.4	10	0.25	..	1 to 2#
b	1	0.4	10	0.5	..	2#
c	1	0.4	10	1	..	Slightly <4#
6a	1	0.4	10**	1	..	2 to 4
b	1	0.4	20	0.5††	..	2 to 4

* Ten milligrams of sodium chloride per cubic centimeter of toxoid was added at the time of adding protamine.

† Nitrogen content of suspension for experiment 2a was 0.065, for 2b, 0.132, and for 2c, 0.10 mg. per cubic centimeter.

‡ After being held at 2 C. (35.6 F.) for two years 1 cc. of suspension which was used in experiment 2a elicited less than 2 units of antitoxin (no smaller quantity was tested for) and 1 cc. of suspension which was used in experiment 2b elicited 3 units. Because of intercurrent infections, only 1 guinea pig immunized with suspension from experiment 2a and only 2 of the group immunized with suspension from experiment 2b at this time survived six weeks.

§ Three cubic centimeters of water was added in experiment 2b and 3 cc. of 0.85 per cent sodium chloride solution in 2c per cubic centimeter of toxoid before adding alum solution.

‖ Three cubic centimeters of 0.85 per cent sodium chloride solution per cubic centimeter of toxoid was added before adding alum solution.

¶ Nitrogen content of suspension was 0.08 mg. per cubic centimeter.

The suspension of protamine toxoid had been held at 2 C. for five months at the time it was used in this experiment.

** Nitrogen content of this suspension was 0.056 mg. per cubic centimeter of suspension.

†† This material was mixed with 0.5 cc. of protamine diphtheria toxoid before injection. Two units of diphtheria antitoxin was produced four weeks after the injection.

cubic centimeter of toxin at the time it was treated with formaldehyde to convert it to toxoid. The hydrogen ion concentration was $10^{-7.2}$; there were 10 Lf units, 2.40 mg. of nitrogen and 10 mg. of sodium chloride per cubic centimeter of finished toxoid. The method of purification seems applicable to the peptone-free

10. Protamine tetanus toxoid has also been prepared from fluid toxoid made in a hog stomach digest medium furnished by Sharp & Dohme, Inc., Glenolden, Pa.

medium of Mueller and his associates[11] and would probably yield a still greater ratio of Lf units to nitrogen if used with toxoid prepared in this medium.

The antitoxin content of the immunized guinea pigs' pooled serums was measured by the subcutaneous lethal test, following the technic of the National Institute of Health[12] and employing standard antitoxin and toxin furnished by that institute as a control and for test doses, respectively. At least 4 guinea pigs were given injections of the preparation under examination and 2 animals received the mixture of serum and toxin at each dosage level tested. The Lf values listed in table 1 are based on the determinations of the Lf units in the original fluid toxoid and that left in the supernate after adding protamine, and were obtained by the procedure of Goldie, Parsons and Bowers.[13] The values can also be obtained by dissolving the final precipitate in a solution of 3 per cent sodium citrate and 5 per cent sodium chloride.

The method for precipitating the toxoid was, in general, as follows (variations will be described in table 1): One milligram of protamine (salmine sulfate) was added for each cubic centimeter of fluid toxoid. About one hour later, before settling had begun, a solution of 0.4 per cent potassium alum ($KA1[SO_4]_2.12H_2O$) was added to adsorb the protamine-toxoid precipitate and to make it easy to disperse the product. The quantity of alum added was, in most cases, equivalent to 0.4 mg. of alum per cubic centimeter of toxoid and, therefore, represents less than 10 per cent of the quantity used in preparing the customary "alum-precipitated" toxoid. The final precipitate was washed with 0.85 per cent solution of sodium chloride and then suspended in the same solution. Variations in details of the general procedure consisted of changing the quantity of protamine or of alum used and, in some instances, changing the ionic strength; the changes were made in order to observe their effect on the ratio of Lf units to nitrogen and on the immunizing efficacy of the finished product.

OBSERVATIONS

Because there are extreme variations in the production of tetanus antitoxin by animals inoculated with the same tetanus preparation,[14] no detailed conclusions can be drawn from tests on small groups of animals immunized at only one dosage level. However, some deductions regarding the influence of the factors just mentioned appear to be justifiable from the experiments. Regardless of the quantity of protamine

11. Mueller, J. H., and Miller, P. A.: Large Scale Production of Tetanus Toxin on Peptone-Free Medium, J. Immunol. **47**:15, 1943. Mueller, J. H.; Schoenbach, E. B.; Jezukawicz, J. J., and Miller, P. A.: The Production of Tetanus Toxin on Peptone-Free Media, J. Clin. Investigation **22**:315, 1943.

12. Rosenau, M. J., and Anderson, J. F.: The Standardization of Tetanus Antitoxin, Hygienic Laboratory Bulletin 43, United States Treasury Department, Public Health Service, 1908.

13. Goldie, H.; Parsons, C. H., and Bowers, M. S.: Titration of Tetanal Toxins, Toxoids and Antitoxins with the Flocculative Test, J. Infect. Dis. **71**:212, 1942.

14. Mueller, J. H.; Seidman, L. R., and Miller, P. A.: A Comparison of Antigenicities of Hydrolysates and Peptone Tetanus Toxoids in the Guinea Pig, J. Clin. Investigation **22**:321, 1943.

used to precipitate the toxoid or of the amount of alum employed to adsorb the complex, every preparation made and tried in guinea pigs was an effective immunizing agent. The use of increasing quantities of protamine seemingly decreased the response to the antigen, since 8, 4 to 6 and 3 units of antitoxin were produced in experiments 1*a*, 1*b* and 1*c*, respectively, in which increasing quantities of salmine were employed. However, in experiment 1*d*, 7 units were produced with the use of the same quantity of protamine (3.5 mg. per cubic centimeter of toxoid) as in experiment 1*c*, the only difference in experimental conditions consisting of the addition of an amount of sodium chloride equal to that already present in the broth. Also, in experiment 5*c*, approximately 4 units of antitoxin were produced under the same conditions as were used in experiment 1*a* (1 mg. of protamine per cubic centimeter of toxoid). It appears nothing is to be gained by adding protamine beyond the amount required to precipitate all the toxoid.

The addition of water resulted in the precipitation of more of the protein derivatives of the broth. This is a consequence of the fact that, as ionic strength is reduced by dilution with water, a given amount of protamine precipitates more of a given protein. Antitoxin production at the dosage level of 1 cc. was unaffected (experiment *2b* compared with experiment *2c*). Therefore, it appears desirable to maintain the sodium chloride content of the fluid toxoid as high as possible, consistent with full precipitation of toxoid at the time of addition of the protamine.

The use of increased amounts of alum (greater than 0.4 mg. per cubic centimeter of toxoid) also tends, by adsorbing nitrogen-containing components of the broth, to raise the nitrogen content of the final product without changing the antitoxin production (experiments *2b* and *2c* compared with experiment *2a*). Also, in experiment 3 it is seen that the use of 1.6 mg. of alum per cubic centimeter of toxoid to adsorb the complex of protamine toxoid did not change the immune response to a dose of 1 cc. of the final suspension from that response observed when 0.4 mg. of alum was used (experiment *3c* compared with experiment *3b*). The considerably higher antitoxin content of the pooled guinea pig serums in experiment 3*a* than in experiment 3*b* (7 units as against 2 to 3 units) may possibly be related to the somewhat greater quantity of toxoid injected or to normal variations in response among different animals. The poor physical condition of the animals which were immunized in experiment 4 may have accounted for the low value of 1 unit of antitoxin produced.

Experiment 5 shows an antitoxin production which happens to be proportional to the quantity of toxoid injected, slightly less than 4 units,

2 units and 1 to 2 units having been formed in response to 1, 0.5 and 0.25 cc. of the protamine-toxoid suspension.

Experiment 6 shows that the injection of a mixture of protamine diphtheria toxoid and protamine tetanus toxoid did not adversely affect the immunizing efficacy of either antigen.

Injection of Protamine Tetanus Toxoid in Children.—Determinations of the quantity of antitoxin present in the serum of children who were given two injections of protamine tetanus toxoid, with an interval of three months between the injections, have been made. The measurements were made at the time of the second injection and again seven and nineteen days after this injection. Unfortunately, the complete experiment has been done on only 4 children. All 4 produced at least

TABLE 2.—*Antitoxin Production by Children Following Injection of Protamine Tetanus Toxoid* *

Units of Antitoxin	No. of Children Who Produced Indicated Titers		
	At Time of Second Injection	7 Days After Second Injection	19 Days After Second Injection
1 or more but less than 10	..	..	1
0.1 or more but less than 1	..	2	3
0.01 or more but less than 0.1	1	1	..
Less than 0.01	7	2	..

* Two injections of 1 cc. each (12Lf) were given with a three month interval. Dr. John J. Miller Jr., of the Department of Pediatrics, Stanford University School of Medicine, did this experiment. Titrations were done by the method of Glenny and Stevens (*J. Roy. Army M. Corps* **70**: 308, 1938). It was not possible to have all the children who were immunized return for blood sampling.

0.1 unit of antitoxin per cubic centimeter of serum in the nineteen day test, a level which is almost surely protective. The complete data are shown in table 2.

COMMENT

There is sufficient experimental evidence to show that protamine will precipitate tetanus toxoid and that when this complex is adsorbed onto a small quantity of alum it is an effective producer of antitoxin. Judging by the fact that all but 1 or 2 per cent of the nitrogen-containing substances of the crude toxoid is left behind, it is to be expected that the final product will give rise to a pronounced reduction in the incidence of reactions following its injection into human beings. An extensive experience with the corresponding protamine diphtheria toxoid [9] further encourages such a belief. It is hoped that many more children will be tested for antitoxin production after immunization with protamine

tetanus toxoid. It is also desirable to know the antitoxin levels after increasing intervals of time following immunization.[15]

It is of importance that our experiments suggest that the final suspension keeps well. It has since been observed that the stability of the protamine-precipitated toxoid can be further improved when the suspension is made up in seventy-fifth-molar phosphate buffer, p_H 7.7., than when an 0.85 per cent solution of sodium chloride is used. More Lf units are found in the former after both have been kept at 37 C. (98.6 F.) to accelerate any deterioration. Finally, it is evident that protamine tetanus and diphtheria toxoids can be mixed without adversely affecting the immunizing action of either.

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15. In the case of protamine diphtheria toxoid 79 per cent of the children had 1/10 unit or more of antitoxin and 60 per cent had 1/5 unit or more two and one-half to three months after the second injection. Between nine and fifteen months after the second dose 90 per cent had 1/10 unit or more and 59 per cent had 1/5 unit or more.[11]

DEFICIENT DEVELOPMENT OF MASCULINITY

A Psychosomatic Problem of Adolescence

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IN ORDER to understand the psychologic disturbances of pubescence and adolescence, it must be borne in mind that the transition from childhood to full physiologic and psychosexual maturity is a particularly trying period.[1] Knowledge is still limited with respect to the interplay of psychologic, organic and growth factors which during the second decade of life have an effect on personality development and may lead to psychosomatic disorders both during adolescence and later in life.[2]

The observations in this report are based on a psychosomatic study of 256 boys whose ages ranged from 9 to 16 years at the initial visit. In all these patients, either the child or a parent expressed concern over the sexual inadequacy of the patient's physique, although there was no evidence of gross congenital defects or endocrine dysfunction and all the boys were capable of eventual development of spontaneous puberty. Some of the somatic complaints were associated with deficiencies in the anatomic and physiologic changes peculiar to the second decade of life, such as apparent inadequacy in the size of penis or testes, or in hair or muscular development or enlargement of the breasts. In other patients, the concern centered on physical characteristics which had always been present but which had acquired an increased significance because of the boy's age. These inadequacies included shortness of stature, obesity, leanness, nevi and deformities of the nose or teeth.

The clinical data have been accumulated since 1935 with an interruption during the war, so that the duration and intensity of the study varied in individual patients.[2a] Personal observation was possible in 68 boys for six months to one year, in 99 boys for one to three years, in

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2. Bruch, H.: Puberty and Adolescence: Psychologic Considerations, in Advances in Pediatrics, New York, Interscience Publishers, Inc., 1948, vol. 3, pp. 219 to 296.

2a. These data were obtained at Babies Hospital, Presbyterian Hospital, Vanderbilt Clinic, Morrisania City Hospital, and New York State Psychiatric Institute and Hospital.

43 boys for three to five years, in 35 boys for five to ten years and in 8 boys for over ten years. The duration of observation was not necessarily indicative of the required length of treatment, as the patients were followed up at intervals to note the effect of or the further need for specific treatment. This report is a preliminary digest of the observations rather than a detailed analysis of each specific problem.

It seems pertinent to this discussion to review the phenomena of growth which, in their dynamic interplay, are considered characteristic for pubescent boys. Usually between the ages of 9 and 14 years, but occasionally even as late as 16 years, genital maturation is associated with a rapid acceleration of growth in height, body breadth and weight, size of the heart, capacity of the lungs and muscular strength. The rapid growth lasts from four and a half to seven and a half years and usually is completed between the ages of 17 and 20 years.[3] There are certain parts of the body which follow another pattern of growth in that nearly the entire growth process occurs during the pubescent and postpubescent periods. While the penis, testes, prostate and pubic and axillary hair show no appreciable growth during childhood, in the period of pubescence they surpass the other parts of the body in velocity of growth,[4] thus emphasizing that adolescence is the period when boys become men.

My observations indicate that the onset of adult sexual interests and the emotional phenomena associated with pubescence correlate highly with maturation of the central nervous system [5] and seem to be related to psychosexual development and the social pressures of cultural patterns rather than to hormone stimulation. Normally, of course, physiologic sexual maturation follows so closely that the heterosexual trends of the person are reenforced by the hormonal influences which manifest themselves during puberty. However, the initial stages of emotional maturation may occur independently of the physical maturation, as has been shown by various studies of eunuchoidism.[6]

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PSYCHOLOGIC DETERMINANTS

It will suffice to outline those psychodynamic factors in psychosexual development which seemed to play an important role in the patients studied. During infancy and early childhood when the child is most dependent on his mother, he may manifest jealousy and hostility toward anyone who shares his mother's affections. These feelings are usually directed against either the father or a sibling and tend to be resolved during subsequent psychosexual development. However, unresolved conflicts may lead to unconscious fear of retaliation,[7] frequently taking the form of castration anxiety. Such anxieties are created by many types of maladjusted parent-child relationships.

Adequate personality development of the child and a normal attitude toward genitality depend not only on the final resolution of these conflicts but also on the standards adopted by the child in building his own identity or ego and on the identifications made in the formation of his superego.[8] In the latent phase of psychosexual development, the grade school age, parents and teachers, who themselves are influenced by cultural patterns and emotional conflicts, have a profound influence on the child's attitudes toward his own body and on his concept of body image. Since the body image, as described by Schilder,[9] is the "picture of our own body which we form in our mind," it is the basis of the individual person's critical evaluation of himself.[10]

PSYCHODYNAMIC FACTORS IN PREPUBESCENCE

I shall attempt to summarize the psychodynamic factors as they were presented in the boys studied in this series. The meaning of any real or assumed inadequacy in adolescent development must be determined by a study of the individual boy and of his family's attitudes as their significance is not inherent in the defect itself. In some adolescent boys the concern over lack of sexual maturity or a possible physical defect is merely a rationalization of the boy's basic feelings of inadequacy which

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10. Curran, F. J., and Frosch, J.: The Body Image in Adolescent Boys, J. Genet. Psychol. **60**:37 (March) 1942.

may date back to earlier childhood.[11] In other boys, such anxiety stems from actual deficiencies in psychobiologic maturation or from distorted concepts of what constitutes normal development in prepubescence.

The attitudes of parents, teachers and playmates encourage prepubescent boys to take pride in their masculine development and frequently impose tyrannic standards of "normalcy" without consideration of basic differences as they occur among individual persons. Many boys with a relatively late onset of puberty are disturbed by serious doubts concerning their own health and adequacies, although their development is well within the limits of normal. They feel abnormal only because they have not attained maximum levels of development. The wish to grow up and to be big is developed in boys through training and imitation, through rivalry with parents and through competition with siblings and companions. Parents have a great influence on the child's attitude toward his own body during childhood, when his concepts of the ideal are formed. During the second decade of life the attitudes of the boy's companions play a decisive role in formulating standards of masculinity. It is at this age that all boys have a great need for acceptance by their peers. Discrepancies between the boy's anatomy and the group's concept of normal are further emphasized by the tendency of the group to call attention to the boy's deficiencies and to make them targets for criticism and disapproval.

Every child has a need for a sense of his own worth, and anything which tends to make him feel inadequate or inferior is apt to be met promptly with some kind of defensive reaction. My findings agree with Ackerman's conclusions that behavioral aberration in boys during the second decade of life is frequently caused by an inadequate adjustment of the feeling of being different.[12] Being different to a child usually implies being inferior.[13] This was also confirmed in a series of 100 junior high school boys studied by Stolz, Jones and Chaffey.[14] They observed that an atypical pattern of sexual maturation constituted an important hazard to wholesome emotional development in 8 of 10 boys who were physically retarded two years or more and in 7 additional boys who exhibited sexually divergent structural characteristics.

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13. Levy, D. M.: Body Interest in Children and Hypochondriasis, Am. J. Psychiat. **12**:295 (Sept.) 1932.

14. Stolz, H. R.; Jones, M. C., and Chaffey, J.: The Junior High School Age, Univ. High School J. **15**:63 (Jan.) 1937.

Psychiatric examination reveals that the most frequent unconscious psychologic mechanism causing anxiety is the acceptance of the failure of development of masculinity as evidence that the castration fear has been realized. Masochistic motivations are frequently found to be woven into the content of such anxieties, the degree of self punishment depending on the degree of guilt and the basic character structure. When boys become inhibited to an extent that normal drives and other satisfactions of successful living are thwarted, conflicts tend to arise and are followed either by direct responses to ideas of worthlessness, inadequacy and self condemnation or by circumvented types of responses giving rise to symptoms of a defensive nature, such as detachment, inordinate dependency or masochistic, paranoid and grandiose strivings.

REPORT OF CASES

CASE 1.—D. K., 14 years 1 month of age, was the older of 2 children and had an intelligence quotient of 110. He was referred for treatment because of shortness of stature and sexual immaturity associated with a personality disturbance manifested by an inability to get along with other boys during the past two years. He was 56 inches (140 cm.) tall and weighed 76 pounds (35 Kg.). His penis measured 4 cm. in length relaxed and 7 cm. in length fully stretched, with a circumference when relaxed of 5 cm. No pubic hair was present (stage 1 [4]). His testes measured 1.5 and 1.5 cc. in volume. In school and on the street he did not play with other boys because he was inept at all athletics. He was frequently pushed around and taunted by the other boys. They called him "baby" or "shrimp," and he would run home crying. He was shy and sensitive and did much crying. He expressed a great part of his resentment through quarreling with his mother, yet, invariably, he would acquiesce to her point of view. He spent much time daydreaming of great personal achievements and figuring out methods of revenge on the boys who taunted him.

His basic personality trend was that of submissive adaptation. He withdrew from ordinary social contacts with children because of anxiety over a real physical inadequacy.

Methyltestosterone U. S. P., 30 mg., was administered by mouth daily for two months. After two months without medication, he was given another course of methyltestosterone. Although this resulted in a spurt of growth, there was no appreciable change in his attitudes. Superficial psychotherapy was then instituted in order to modify the attitudes of both the parents and the patient and to establish a sense of security in the child. In three months of combined therapy he made remarkable progress in his attitudes, as well as in his physical appearance. At 15 years of age he was 61 inches (153 cm.) tall and weighed 91 pounds (41 Kg.). His penis measured 6 cm. in length relaxed, 9 cm. when fully stretched and 6 cm. in circumference. His testes measured 3 and 2.5 cc. in volume; pubic hair was present. He was also rapidly acquiring a genuine feeling of security. At present, he is 16 years of age and appears well adjusted at home and at school.

The psychodynamics of devaluated self esteem lie in the intense feeling of helplessness and isolation that result from the discovery of "self" as an undesirable, inept, inadequate and contemptible person.

Subsequent situations in which such an adolescent feels worthless may precipitate an anxiety reaction or any variety of psychosomatic complaints. It is well known that boys of this age are vulnerable to slights and to criticism or disapproval. In a setting of overevaluation of the opinion of others so characteristic of adolescents such vulnerability makes life a constant source of pain.[12]

CASE 2.—T. L., one member of a set of 15 year old dizygotic twins was referred for treatment because of emotional problems associated with his failure to develop puberty. The basic problem evolved from the fact that the patient had always been the larger of the twins until his brother entered puberty one year before. From that time the brother matured progressively, while the patient retained his childish physique. T. L. was 63¾ inches (161 cm.) tall and weighed 85 pounds (38.6 Kg.). His penis measured 4 cm. long relaxed and 7 cm. long fully stretched, with a circumference of 4.5 cm. His testes were each 1 cc. in volume. No pubic hair was present (stage 1). His brother, however, was 64½ inches (163 cm.) tall and weighed 106 pounds (48 Kg.); his penis was 7 cm. long relaxed, 12 cm. long fully stretched and 7 cm. in circumference, while his testes were both 5 cc. in volume; pubic hair and muscular development were well advanced (stage 4).

The retarded twin reacted by being stubborn, destructive, mischievous and domineering. At school and summer camp and on the playground he continually attempted to divert attention from his brother, who excelled in all sports, in order to become the center of attention by childish antics. He irritated and annoyed adults apparently as a result of his feeling of futility. Since he could not please anyone, he contrived to arouse some positive reactions even though they were antagonistic.

Psychiatric examination revealed adequate adjustment and apparently normal psychosexual development during infancy and early childhood. However, with the advent of his twin brother's puberty and his own failure to mature, the normal sibling rivalry was intensified. He reverted for an explanation for his "punishment" to the normal conflicts and hostility of childhood and thereby rekindled the castration anxiety.

The patient received a three month course of treatment with 30 mg. of methyltestosterone daily by mouth. After a two month period of rest, he was given a second course. Throughout this time he received psychotherapy aimed at rebuilding his self esteem. This combined routine of hormone induction of pubescence and psychotherapy was followed by remarkable changes in his personality which progressed even more rapidly than his physical maturation. One year has passed since the onset of treatment, and he now is well adjusted at home, in school and on the ball field. He has learned to accept his brother's physical superiority and enjoys his brother's success in athletics. He is functioning at a realistic level and has utilized his own assets, even though he still has not progressed beyond the early stages of pubescence, while his brother has fully matured.

In many of those boys showing a relative delay in sexual maturation, feelings of inadequacy were observed to persist when spontaneous pubescence was established without concomitant psychotherapy. Kinsey

and his co-workers [15] supported this finding with the statement that the "life time patterns of sexual behavior are greatly affected by the age of onset of sexual maturation." Late-maturing boys appear to have an appreciably lower level of sexual activity throughout life than the earlier-maturing boys.

Many children in their second decade who have not matured adequately are not fully aware of their self contempt, for the defensive forces of the ego tend to set up compensatory mechanisms to avert anxiety.[16] A common defense reaction leads to complete repression of feelings of inferiority and to a subsequent swing to superior strivings, embracing compulsive drives for dominance, mastery and power. It will always be possible, however, to relate expressions of this narcissistic inflation to basic feelings of helplessness. One of the unfortunate consequences of grandiose striving will usually be that the patient sets up goals for himself which are impossible for any person to achieve. Repeated failures reenforce the conviction of worthlessness and, thus, continue the vicious cycle of grandiose strivings.

These trends which have been discussed are present both in the group of boys in whom a primary psychoneurotic disturbance leads to rationalized thoughts of sexual inadequacy and in the group of boys in whom loss of self esteem is secondary to actual sexually divergent structural characteristics. The problem of rebuilding the child's devaluated self esteem is vitally important, because it is impossible for any person to attain mental health without a wholesome attitude toward himself as a human being.[17]

Case 3.—A. C., a boy 14 years 6 months of age, of normal intelligence, was referred for treatment because of shortness of stature, sexual immaturity and overaggressiveness. He was 58 inches (145 cm.) tall and weighed 82½ pounds (37.4 Kg.). His penis measured 5 cm. in length relaxed, 7 cm. in length fully stretched and 4.5 cm. in circumference relaxed. The testes measured 1 and 1.5 cc. in volume. No pubic hair was present (stage 1[4]). In contradiction to the first patient (case 1) this boy was hostile, aggressive, destructive and truant from school. He indulged in petty thievery and was domineering at home. Since he was able to demand respect and obedience from other boys, he organized a local gang and barely missed getting into serious difficulties.

Psychiatric examination disclosed that he had the same unconscious attitudes of submissive adaptation and anxieties as D. K., although he overcompensated in the direction of overaggression. He felt the need of being a leader in all activities. Criticism by any of the other boys would result in a severe anxiety reaction which was disguised by a display of rage or temper.

15. Kinsey, A. C.; Pomeroy, W. B., and Martin, C. E.: Sexual Behavior in the Human Male, Philadelphia, W. B. Saunders Company, 1948, pp. 218 to 226.

16. Wile I. S.: The Challenge of Adolescence, New York, Greenberg, Publisher, Inc., 1939, p. 177.

17. Adolescence, in the Forty-Third Yearbook, National Society for the Study of Education, 1944, University of Chicago, Department of Education, pt. 1, chap. 5.

Therapy was initiated in both the physiologic and the psychologic spheres and resulted in decided improvement in his behavior, as well as in his maturation, even though his growth spurt was not remarkable. At 16 years of age, he was 60 inches (151 cm.) tall and weighed 95 pounds (43.2 Kg.). His penis measured 6 cm. in length relaxed, 10 cm. in length fully stretched and 7 cm. in circumference. The volume of the testes was 3 and 4 cc. Pubic hair was present (stage 4).

PSYCHOTHERAPY

The concept of body-mind unity does not imply that either component is dominant in the development of human personality. Both contribute equally to the organization of the personality and should be utilized for the management of the individual child.[18] Adequate treatment of a prepubescent boy showing an inappropriate masculine physique in association with a personality disorder frequently requires, in addition to psychotherapy, hormone induction of pubescence. In these boys hormone therapy is not given because of any evidence of endocrine dyscrasia but rather as an adjuvant to psychotherapy. In a few patients it may be necessary to resort to plastic surgical treatment to alleviate the physical defect initiating the anxiety reaction.

The extent of psychotherapy required varies. For many boys the pediatrician is well capable of managing the problem but for others specialized training and skill are required. Reassurance was considered sufficient in about 25 per cent of the boys studied. However, when psychoneurotic conflicts are already well advanced, reassurance generally falls short of its therapeutic goal, and it becomes necessary to turn to more methodical psychotherapeutic procedures.[19]

Case 4.—J. K. was representative of the group of boys in which both parent and boy merely required reassurance. He was 13 years of age, weighed 99 pounds (45.1 Kg.) and was 60½ inches (53 cm.) tall, both measurements being at about the 50 percentile level. His penis measured 4 cm. in length relaxed, 9 cm. in length fully stretched and 5 cm. in circumference relaxed. Each testis measured 1.25 cc. in volume, a value at about the 40 percentile level. In spite of these normal measurements his mother's chief complaint was that he was not "manly" and that his penis had not grown since infancy. The boy had no interest in sports and was inclined to spend much of his time drawing and reading. A psychiatric survey revealed that the basic problem was the mother's own frustration arising from a feeling of insecurity in her sexual role. She projected her concern about her sexual adequacy to her son. She examined him repeatedly while he was bathing or dressing and expressed anxiety over his failure to mature, thus creating in the boy insecurity and concern about his sexual adequacy.

When the case came to my attention, both the mother and the boy required psychotherapy. An attempt was made to evaluate and resolve her conflicts and to alleviate the boy's anxieties and feelings of insecurity. Hormone

18. Lurie, L. A.: Somatopsychic Aspects of Behavior Disorders of Children, M. Clin. North America **31**:668 (May) 1947.

19. Levy, D. M.: Attitude Therapy, Am. J. Orthopsychiat. **7**:103 (Jan.) 1937.

induction of pubescence did not seem indicated because the mother and the boy accepted the assurance of the therapeutist that the boy was physically well and within normal limits of genital size and that he would mature spontaneously, which he did while under observation.

If the boy's expectations of himself are not too exorbitant, it may be possible to rebuild his entire estimate of himself by activities of creative nature. This requires a rebuilding of self confidence and the reassurance that he can function independently without the need of a magical protector and without the fear of being hurt. Directive therapy, part time work, modification of the school program and externalization of interests into such channels as hobbies and social activities may rebuild self esteem through achievements and thereby serve to enhance the concepts of the body image. If congenital defects, scars or chronic disabling diseases preclude an alteration of the condition, the inculcation of stoicism becomes the immediate therapeutic aim. Psychotherapy should then be directed toward building up an attitude of self acceptance.

Avoid psychotherapeutic attempts aimed merely at exposing the depth and destructiveness of the patient's contemptuous image of himself as they are both ineffectual and dangerous. Similarly, abrupt removal of his protective devices, such as a tendency to dominancy, power strivings and perfectionism, may precipitate panic, for they are defensive mechanisms which shield him from helplessness and isolation. Moreover, merely a discussion of intrafamily conflicts may provide such a boy with a scapegoat to which he may shift responsibility for his condition.

The most effective therapeutic procedure is a process of reeducation accomplished by psychotherapy along psychoanalytic lines. Through the establishment of an interpersonal relationship between the patient and his psychotherapeutist, the boy's character structure unfolds, and the symbols by which he measures his estimate of himself are reevaluated as he experiences them actively. The extent of the reevaluation of the self is related to the ability of the patient to gain insight into his character structure and to reorient himself to others. Orthodox analysts have adopted a pessimistic attitude toward the advisability of treatment during pubescence or adolescence and have recommended a wait until the "personality struggle has congealed into its adult mould." [8a] Other therapeutists, such as Ackerman [12] and Curran,[20] have argued the opposite view with equal conviction. I believe that pubescence and adolescence are promising periods for psychotherapy. The personality

20. Curran, F. J., and Schilder, P.: Constructive Approach to Problems of Childhood and Adolescence (Survey of Studies from Children's and Adolescents' Ward in Bellevue Psychiatric Hospital, New York City), J. Crim. Psychopath. **2**:125 (Oct,) 1940; **2**:305 (Jan.) 1941.

of the child in the second decade, being dynamic and open to suggestion, is highly amenable to all external influences, including those of psychotherapy. However, it is frequently necessary to modify one's approach according to the needs of the individual child. A modified form of play analysis is effective in younger boys and mutual discussions, rather than formal psychoanalytic sessions, are recommended for older boys. Projective technics, drawings, finger painting and story completion methods, are also utilized with varying success. The same is true for collective discussions in small groups. The duration and intensity of active psychotherapy seem to be less and the results more spectacular than they are in cases of psychoneurosis of corresponding intensity in adults. This is particularly true in boys in whom it is possible to modify the traumatic aspects of the situation, namely, the inadequacy of their masculine physique.

HORMONE INDUCTION OF PUBERTY

Another part of the management of undeveloped boys is directed toward the physical aspects of their deficiency. While psychotherapy is essential in their emotional readjustment, it cannot be expected to alter the bodily defects which initiate the series of experiences responsible for their conflicts. The aim of somatic treatment is to correct the physical inadequacies in order to enhance, or at least to avert further loss of, self esteem. Although many phenomena of adolescence which are commonly regarded as endocrine abnormalities are merely physiologic variations in the process of maturation [21] and although there is a wide range of variability in different constitutional types, so that in due time the boys develop into normal adults without hormone therapy, in many cases I have found hormone induction of pubescence an important adjuvant to psychotherapy. Short stature, poor muscular development and failure of genital growth are the usual indications of delayed onset of pubescence. Any combination of these disturbances may lead to the boy's loss of self esteem and may be helped through this method of induction of pubescence. However, hormone induction of pubescence alone is not adequate,[22] as it may serve to substantiate the boy's feeling of inadequacy unless psychotherapy is given along with it.

Potent hormones have been available in the latter part of this study in the form of methyltestosterone, in addition to the chorionic gonado-

21. Shorr, E.: Endocrine Problems in Adolescence, J. Pediat. **19**:327 (Sept.) 1941.

22. Rubinstein, H. S.: Treatment of Hypogonadism (Combined Use of Testosterone Proprionate and Psychiatry in Treatment of Hypogonadal Behavior Problem Boys), J. Clin. Endocrinol. **2**:519 (Aug.) 1940; Endocrine Therapy in Neuropsychiatric Disorders, Dis. Nerv. System **3**:399 (Dec.) 1942.

tropins.[23] In the beginning, injections of testosterone propionate were used. Methyltestosterone is usually given by mouth, 20 to 30 mg. daily, for a period of two or three months, although evidences of gonadal response are noted within one or two weeks. In some patients this minimal response is adequate and hormone treatment is discontinued in one month, but usually at least a two month course of treatment is given. After two months of hormone therapy, it is discontinued for about two months, at the end of which time another course is given. If the primary goal is stimulation of growth in height, enough time should elapse between courses to permit partial recession of the effects on end organs, in order to allow several courses of treatment before puberty is finally induced. However, if height is not the primary concern, treatment may be given more continuously [24] until midpuberty (stage 3 or 4 [4]). At this stage pubic hair is developed at the base of the penis, axillary hair first appears, the penis measures 8 to 12 cm. in length fully stretched and 5 to 6 cm. in circumference and the testes measure 2.5 to 5 cc. in volume. Only when treatment is prolonged should chorionic gonadotropins be given to stimulate the testes to avoid their growth from lagging too far behind that of the penis and the development of secondary sex characteristics. In the group of patients treated in this intermittent manner it was possible to complete the follow-up observation of more than 50 boys, and no gross evidence was found either of any deleterious effect on the testes or of stunting of growth by early fusion of the epiphyses.

MISCELLANEOUS PROBLEMS

Obesity is a problem in itself. Much has already been written on the psychologic origin of obesity and the behavior pattern associated with it.[25] Since obesity in boys involves the chest, abdomen, thighs

23. The Schering Corporation, Bloomfield, N. J., made available a grant for statistical and clerical help and supplied the hormone preparations used in this study.

24. Schonfeld, W. A.: Management of Male Pubescence, J. A. M. A. **121**:177 (Jan. 16) 1943.

25. Levy, D. M.: Aggressive-Submissive Behavior and the Fröhlich Syndrome, Arch. Neurol. & Psychiat. **36**:991 (Nov.) 1936. Mittelmann, B.: Juvenile Adiposogenital Dystrophy: Neurologic and Psychopathologic Aspects; Results of Organotherapy and Psychotherapy, Endocrinology **23**:637 (Nov.) 1938. Bruch, H.: Obesity in Childhood: Physiologic and Psychologic Aspects of the Food Intake of Obese Children, Am. J. Dis. Child. **59**:739 (April) 1940. Bruch, H., and Touraine, G.: Obesity in Childhood: The Family Frame of Obese Children, Psychosom. Med. **2**:141, 1940. Bruch, H.: Obesity in Childhood and Personality Development, Am. J. Orthopsychiat. **11**:467 (July) 1941; Obesity in Childhood and Endocrine Treatment, J. Pediat. **18**:36 (Jan.) 1941; Obesity in Relation to Puberty, ibid. **19**:365 (Sept.) 1941.

and buttocks, it is frequently thought of as a female distribution of fat. Therefore, the boy is erroneously accused of "feminization." This, in association with the fact that the penis is usually surrounded by suprapubic fat, thus appearing smaller than it actually is, further supports the contention of inadequate sexual development. This condition carries with it the threat of eunuchoidism and may lead to a mistaken diagnosis of Froehlich's syndrome. Therapeutic management of these boys requires reduction of weight by diet, increased physical activity and use of amphetamine (benzedrine®) sulfate in addition to psychotherapy. The child should be encouraged to become independent and self reliant and to make constructive use of his physical and mental endowments, so that he may find more dynamic outlets for his creative drives than the static form of "physical largeness." Obesity in prepubescence is usually a somatic manifestation of an emotional conflict in a constitutionally predisposed person, rather than a symptom of endocrine dysfunction. Actually, obese boys usually mature earlier than do boys with normal weight. However, the mother and child are frequently reluctant to accept the fact that the boy's genital status is normal, if not advanced, for his age.

Plastic surgery was found helpful for a few boys with gynecomastia which persisted after puberty was established. Mastectomies were performed by means of a special technic, devised by Dr. Jerome P. Webster, which left no noticeable scar.[26] The plastic surgeon was also of great help in building up the self esteem of some of the boys by removing disfiguring scars and by correcting nasal deformities after the establishment of puberty. The orthodontist contributed to the relief of anxieties through correction of dental deformities. The cooperation of the surgeon and the urologist was useful in boys who required correction of cryptorchism through orchiopexy. However, any failure in the surgical attempt to bring the testes into the scrotum may lead to increased anxieties and feelings of futility.

SUMMARY

This report is based on the developmental and psychiatric evaluation of 256 boys who ranged in age from 9 to 16 years at the initial visit and who were followed for six months to twelve years. The boys presented personality difficulties and emotional conflicts due to fears of physical inadequacy.

Many of the variations in puberal development commonly regarded as endocrine abnormalities are genetically determined physiologic variations in the process of maturation and fall within the limits of normal

26. Webster, J. P.: Mastectomy for Gynecomastia Through a Semicircular Intra-Areolar Incision, Ann. Surg. **124**:557 (Sept.) 1946.

variability. However, an apparent or actual delay in the age of onset of sexual maturation, the failure of initiation of the growth spurt of pubescence or an inadequacy in masculine development may lead to a variety of personality conflicts and psychosomatic complaints in the early part of the second decade of life. The psychodynamics associated with these personality disorders vary in individual boys. Castration anxieties and feelings of inadequacy play an essential role in the unconscious mechanisms involved. However, conscious motivations seem equally important in a child of this age group and are usually related to the boy's dependence on approval by his companions. Deviation from the group pattern leads to increased feelings of inadequacy with subsequent loss of self esteem.

Treatment is discussed from both a psychiatric and a somatic point of view, with emphasis on the need for improving the bodily defects responsible for the emotional conflicts. Physical treatment may consist of hormone induction of pubescence or use of plastic surgical methods and is to be regarded as an essential adjuvant to psychotherapeutic procedures. The proper application of psychotherapy remains the mainstay of treatment.

62 Waller Avenue.

EXCISIONAL SURGICAL TREATMENT OF PULMONARY TUBERCULOSIS IN CHILDREN

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PNEUMONECTOMY, or resection of the diseased lung, in the treatment of pulmonary tuberculosis in adults is now an accepted procedure, although indications for its employment remain controversial. While pneumonectomies have been performed in children, mainly for bronchiectasis, we were unable to find, in a review of the literature, cases of pulmonary tuberculosis treated in this manner. There are, however, brief references to lobectomies in the treatment of this disease in persons in the growing age period, with apparent success.[1]

As the disease in children usually does not progress to the stage that makes this form of therapy necessary, reports can be presented on only 4 patients in whom pneumonectomy was performed since November 1946 for pulmonary tuberculosis. The children ranged in age from 3 to 13 years at the time of operation.

The operation in children presents problems not encountered in adults. Obliteration of the residual "dead space" created by the pneumonectomy must be approached from other points of view. There are technical difficulties at the time of the surgical procedure that may not be present in the adult patient. Last, the disease in children differs sufficiently from that in adults to make new criteria for excisional surgical treatment necessary.

This paper is presented to illustrate a new approach in the treatment of those children who do not respond to conservative methods or in whom such therapy is expected to fail.

From the Departments of Pediatrics (Bret Ratner, M.D., director) and Thoracic Surgery (Louis R. Davidson, M.D., director) of Sea View Hospital, Staten Island, N. Y.

1. Doyen, E., in the proceedings of the Congrès français de chirurgie, Paris, 1895, p. 195; cited by Jones, J. C., and Dolley, F. S.: Lobectomy and Pneumonectomy in Pulmonary Tuberculosis, J. Thoracic Surg. **8**:351, 1939.

REPORT OF CASES

CASE 1.—D. N., an adolescent Negro girl 12 years of age (born Feb. 16, 1934), was admitted to Sea View Hospital, Staten Island, N. Y., on April 9, 1946, with a history of onset of her disease in February 1946. On her admission, her sputum contained acid-fast bacilli and roentgenograms revealed a cavity in the upper lobe of the left lung, with infiltration throughout the remainder of the left lung and productive dissemination in the right midpulmonary field. On April 18, pneumothorax was initiated on the left side, and on August 8 an attempted internal pneumonolysis was unsuccessful. The collapse was ineffectual and, therefore, the pneumothorax was abandoned (fig. 1 *A*). On November 12, pneumonectomy on the left was performed, despite an exudative lesion in the right midpulmonary field, which was recognized at the time the decision was made to treat this patient with the excisional surgical method. No thoracoplasty followed the pneumonectomy because of the danger of severe scoliosis.

The patient's sputum became negative for tubercle bacilli for a short while. On Feb. 26, 1947, a suspicious cavity was noted in the right lung, at the site of

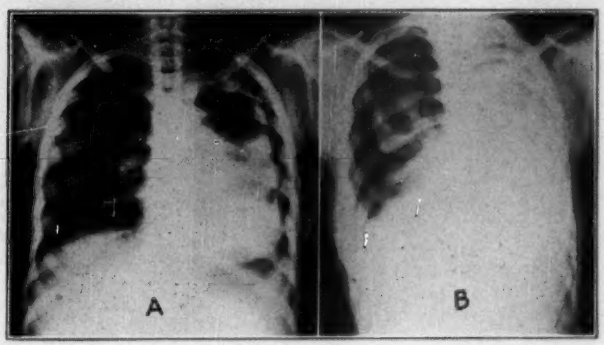

Fig. 1 (case 1).—Roentgenograms (*A*) taken before operation, showing almost complete destruction of left lung with abandoned and ineffective left pneumothorax, and (*B*) taken after pneumonectomy on the left, showing right pneumothorax. The patient was breathing with 20 to 25 per cent of normal lung volume.

the previously described exudative area and the sputum became positive shortly thereafter. The patient then, for the first time, received a course of treatment with streptomycin for several months, without any change in her status.

Pneumothorax was subsequently initiated on the right side on September 24. Thoracoscopy and internal pneumonolysis were done on November 7. Lysis of one broad adhesion permitted 50 per cent collapse of the right lung (fig. 1 *B*). However, the cavity was of the so-called tension type and, as the pneumothorax was increased, the cavity became larger. This form of therapy was, therefore, abandoned.

After considerable delay, due to the patient's reluctance to accept further surgical treatment, and after some additional noncavitary spread of the disease on the right, a two stage open cavernostomy was done on July 16 and Aug. 6, 1948. In spite of this, the patient's sputum continued to yield tubercle bacilli. She died on March 1, 1949 because of progression of her tuberculosis.

A surgical specimen revealed caseous bronchopneumonia within which were present multiple large cavities. Acinous nodose and encapsulated caseous foci were observed throughout the upper and lower lobes of both lungs.

Pulmonary fibrosis was present throughout and practically no functioning pulmonary tissue remained. The tracheobronchial lymph nodes were involved with a tuberculous process.

CASE 2.—L. C., a Negro girl, was admitted to Sea View Hospital on May 25, 1948 at 11 years of age, having been transferred from another hospital. Her illness presumably began in November 1947, when her brother was sent to the hospital with pneumonia, which later proved to be tuberculosis. The disease progressed rapidly and the brother died shortly after his transfer to Sea View Hospital. A roentgenogram of the patient's chest at the time of her brother's hospitalization revealed bilateral hilar adenopathy. She never appeared sick, and her illness was discovered only on a routine check by the city health department. She was hos-

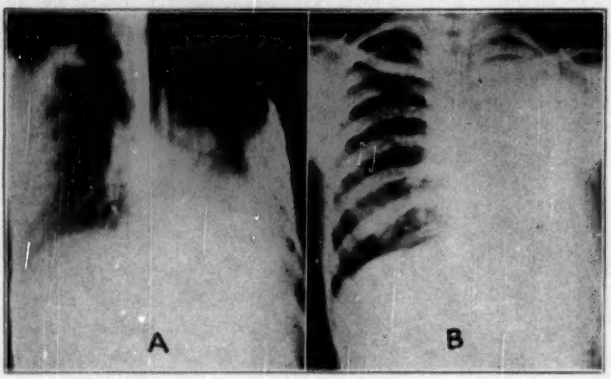

Fig. 2 (case 2).—*A*, tomogram taken before operation showing cavity in lower lobe of left lung. *B*, roentgenogram taken after operation showing beginning of mediastinal shift.

pitalized in March 1948, at which time roentgenologic study revealed widespread infiltration of the left lung, with cavitation at the third interspace. She was transferred to Sea View Hospital in May 1948. On her admission the gastric washings and feces showed acid-fast bacilli and the Mantoux reaction (1:10,000) was positive. A roentgenogram at that time showed advanced caseous, pneumonic infiltration of the entire left lung, with partial consolidation and a large irregular cavity in the dorsal segment of the lower lobe (fig. 2*A*). The right lung was normal. Because of the severe, nonfibrosing, rapidly spreading lesion, pneumonectomy was performed on June 11. The postoperative course was excellent. Penicillin and streptomycin were given before and after the operation. Gastric washings became negative for tuberculosis organisms and have remained so. When last seen, on March 1, 1949, she was attending public school full time and leading a normal life. She was asymptomatic and a roentgenogram of the lung revealed no change in her status (fig. 2*B*).

Pathologic Report on Excised Lung.—Throughout the upper lobe there were numerous single and confluent excavations, measuring 0.2 to 1 cm., following the bronchial tree. The remainder of the lobe was resilient, but scattered throughout there were acinous nodose foci (0.1 to 0.2 cm. in diameter). In the lower lobe there was a cavitation, 2 by 3 cm., in the posterior basal segment reaching 0.5 cm. from the lateral pleura. There was no attempt at encapsulation, and the caseous process extended irregularly into the surrounding tissue. The rest of the lower lobe contained the same type of multiple confluent cavitations as were seen in the upper lobe. Little functioning pulmonary tissue was evident.

Case 3.—S. G., a 4 year old Puerto Rican girl (born Nov. 1, 1943), was admitted to Sea View Hospital on April 2, 1948. There was no history of contact with tuberculosis. On her admission, a tuberculin reaction was positive and gastric washings contained acid-fast bacilli, but no cavitation could be demonstrated roentgenologically until May 14, when tomography revealed a cavity 1.5 cm. in diameter in the mesial portion of the lower lobe of the left lung. Bronchoscopy on May 5 had shown no lesions. Artificial pneumothorax was successfully initiated on June 11, with 80 per cent collapse of the lung. Despite this, the cavity continued to be persistently visible and on fluoroscopy there appeared to be diaphragmatic

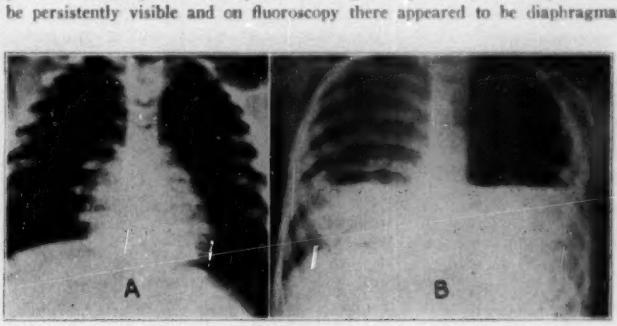

Fig. 3 (case 3).—*A*, Bucky roentgenogram taken before operation demonstrating cavitary disease in lower lobe of left lung behind cardiac shadow. *B*, roentgenogram taken after pneumonectomy showing hernial defect encroaching on contralateral lung (right) with fluid level due to left pleural effusion.

adhesions preventing further collapse of the lower lobe of the left lung (fig 3*A*). The gastric washings, which had become negative for tuberculosis organisms during the preceding two months, were repeatedly positive throughout July and August. Streptomycin (0.5 Gm. daily) was given intramuscularly from July 20 until September 27. In October a second cavity was noted in the lower lobe of the left lung. On November 16, it was decided to excise the lower lobe of the left lung, but at the time of operation it was noted that the pathologic changes had extended beyond the fissure and excision of the left lung was deemed more advisable. Enlarged nodes interfered with the surgical procedure. At the time of operation, it was noted that the left parietal pleura herniated across the mediastinum into the right side of the chest. Immediately after the operation fluid from the pleural effusion on the left side was seen in the hernial sac on the right (fig. 3*B*). The hernial sac encroached considerably on the contralateral lung but did not impair the patient's recovery. She was given streptomycin and penicillin before and after the operation. Since the operation, all gastric washings have been negative for tubercle bacilli. The patient is up and about, and the disease is considered arrested.

Examination of the excised left lung revealed the lower lobe to be largely involved with caseous bronchopneumonia, within which a cavity was present in the basal aspect. The upper lobe was relatively free of disease except for a small area immediately adjacent to the interlobar fissure, consisting of encapsulated caseous foci. Endobronchial and lymph node tuberculosis was also present.

CASE 4.—J. T., a Negro boy 2½ years of age (born Jan. 17, 1946), became ill in August 1948, with fatigue and cough for several days. On his admission to another hospital, roentgenologic examination revealed hilar adenopathy and infiltration of the middle and lower lobes of the right lung. The Mantoux reaction was strongly positive, and the patient was sent to Sea View Hospital on November 14. Past and family histories were noncontributory. On his admission gastric washings and feces contained no acid-fast bacilli. A roentgenogram showed extensive consolidation of the middle and lower lobes of the right lung, with the middle lobe fairly homogeneously consolidated. There was a well defined, comma-shaped collection of air in the outer third of the right lung (fig. 4*A*). The left lung appeared normal. Subsequent films, including tomograms, showed a well defined

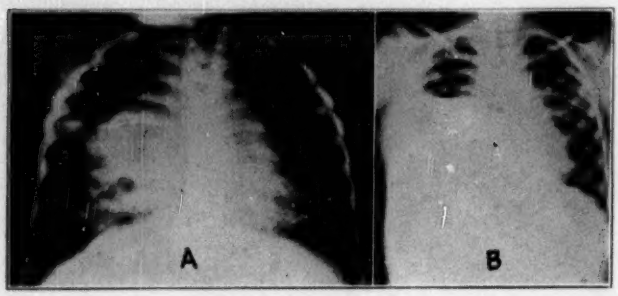

Fig. 4 (case 4).—*A*, roentgenogram taken before operation showing large, comma-shaped collection of air. This ultimately proved to be a cavity in the lower lobe of the right lung. *B*, roentgenogram taken seven days after pneumonectomy.

cavity in the dorsal apical segment of the lower lobe of the right lung, with suspicious small satellite areas of cavitation. There was considerable widening of the mediastinal shadow, especially to the right. Sixteen gastric washings, over a period of two months, revealed no tubercle bacilli.

The patient was afebrile on his admission and remained so for one week, when the temperature rose to 103 F. and there was increased dulness to percussion over the midportion of the right lung posteriorly. The breath sounds were distant. The patient improved clinically, but the physical signs persisted. Bronchoscopy produced white caseous material from the right main bronchus which was positive for tubercle bacilli. On December 31 pneumonectomy on the right was done. A lobectomy was attempted but was not done because of interference by the tracheobronchial nodes which made the procedure technically too difficult. The postoperative condition was good (fig. 4*B*). The patient's temperature rose to 101 F. but subsided within a few days. Diagnostic thoracentesis was performed nine days after the operation and 50 cc. of reddish brown fluid was withdrawn, which yielded

no tubercle bacilli on smear or culture. All subsequent gastric washings have remained negative. Except for chickenpox on Jan. 14, 1949, the patient's recovery was entirely uneventful, and he is asymptomatic at present.

The excised lung revealed complete caseous bronchopneumonia of the middle and lower lobes of the right lung and a large cavity in the dorsal segment of the lower lobe, with several smaller cavities beneath it. The bronchus to the lower and middle lobes revealed endobronchial tuberculosis. The upper lobe of the right lung appeared normal and the tracheobronchial lymph nodes were involved with a tuberculous process.

COMMENT

Reports have been presented on 4 children in whom pneumonectomy was performed for pulmonary tuberculosis. Three are well. They are asymptomatic and their gastric washings repeatedly contained no acid-fast bacilli. In 1 patient, progression of the tuberculous process continued. This represents a rate of 75 per cent with arrested cases, a figure which is consistent with the over-all statistics for adults at Sea View Hospital. It is extremely doubtful that any of these patients would have survived if other forms of therapy had been used.

Three patients were girls. There were 1 Puerto Rican and 3 Negro patients. This may fit in with observations that primary complexes are larger in Negro children. The pulmonary findings in children of this race oftener fit the description of the "progressive primary complex" than those in white children. [2] The pathologic observations in 3 patients (cases 2, 3 and, possibly, 4) indicate that the lesions may fit in the latter category.

The operation was on the left side in 3 of the patients. This is consistent with the findings in adults, most series of whom show more pneumonectomies on the left side.[3]

Analysis of case 1 reveals the following possible causes of failure:

1. An exudative lesion was present in the contralateral lung at the time of surgical treatment. This was recognized then, but, since the patient's prognosis was hopeless and since many exudative lesions heal spontaneously, it was decided to proceed with surgical intervention. Control of the pathologic process on the more involved side often has a favorable influence on a contralateral lesion.[4] Also to be considered was the fact that no other form of therapy was available to this patient.

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2. Auerbach, O.: Tuberculosis in Children, Am. J. Dis. Child. **75**:555 (April) 1948.

3. Gilbert, L.: Pulmonary Resection for Tuberculosis, Quarterly Bull., Sea View Hosp. **9**:222, 1947.

4. Bernou, A.; Véran, P., and Marécaux, L.: Favorable Contralateral Effect of Unilateral Thoracoplasty in Pulmonary Tuberculosis, Rev. de la tuberc. **4**:579, 1938. Brugger, H.: Collapse Treatment of Open Tuberculosis in Children and Youthful Persons, Monatsschr. f. Kinderh. **79**:393, 1939.

2. The surgical procedure was performed without the protective and beneficial effects of streptomycin.

3. At the time of surgical treatment, the patient was in the adolescent period, at best a dangerous age for the spread of tuberculous lesions. She lived more than two and a half years following pulmonary surgical intervention and it is questionable that this survival would have been possible with other therapy.

The remaining patients had clear contralateral lungs on both roentgenograms and physical examination. The conditions of these patients were ideal for surgical treatment and they have done well. Children, in particular, are well suited for this procedure because they tolerate both the anesthesia and the operation better than do adults. Their recovery period is shorter and smoother, and they can stand a greater loss of pulmonary tissue. This was evident in all 4 children, who immediately after operation presented no difficulty.

One patient (case 3) required thoracentesis for pleural effusion on one occasion. Taps were made on the other patients for diagnostic purposes only. Shifting of the mediastinum to obliterate the pleural cavity on the side operated on commenced early. The large hernial defect in 1 patient (case 3) had no influence on the course, although the defect encroached considerably on the contralateral lung. This is consistent with the previous statement that children can tolerate the loss of greater amounts of pulmonary tissue than adults. In another patient (case 1), after the pneumonectomy, contralateral pneumothorax was induced and pushed to the point where, at one time, the patient was functioning with 20 to 25 per cent of normal lung volume (fig. 1 *B*).

The body temperatures of all patients rose after the operation—the younger the patient, the higher the rise—but all returned to an afebrile state in a short time. One patient (case 2) was febrile before operation, with a temperature up to 102 F., but by the third postoperative day she was afebrile.

The indication for surgical treatment in 2 patients (cases 1 and 2) was "destroyed lungs" while in the other 2 patients (cases 3 and 4) it was cavities of the basal lobe. The cases of the first 2 would also fit the classification of desperate risk, since no other form of therapy was available. In 1 patient (case 4), a lobectomy, rather than a pneumonectomy, may have sufficed but this was not done for technical reasons. The small size of the child and the enlarged nodes which ruptured during the operation interfered with the surgical technic.

It would be of distinct advantage to save as much good lung as possible. In the first patient (case 1), had a lobectomy been performed, a segmental resection or lobectomy might have been possible on the contralateral side. However, the extent of the pathologic involvement precluded this.

The ipsilateral pleural effusion following surgical treatment was never a problem; in only 1 patient was a tap required and this was undoubtedly because of the presence of the hernia. The only indication for thoracentesis is dyspnea, and not mediastinal shift or sterile fluid.

It is difficult to set down criteria for this operation for patients of the pediatric age group. In adults, many surgeons feel that resectional surgical therapy should not be advised in competition with common collapse measures but should be held in reserve for those patients in whom such measures have failed or are expected to fail.[5] In children, such a view is perhaps questionable. Thoracoplasty, so often used in adults with good results, is definitely contraindicated in persons of the growing age period because of the extreme deformity which inevitably results.[6]

Pneumothorax was attempted in 2 of the present patients (cases 1 and 3) without success. In 1 patient (case 2), because the lesion was expanding so rapidly and because the cavity was in the dorsal segment of the lower lobe of the left lung, a site often resistant to pneumothorax therapy, it was decided to operate at once. In another patient (case 3) the cavity was large and was located in an area where less radical therapy was expected to fail, and in fact did fail. In the last patient (case 4), the site of the pathologic lesion was also the prime factor in the early performance of the surgical procedure.

Overholt and Wilson[7] stated that if this form of therapy is to be used it should be done early enough to prevent the extension of the disease beyond the original site, before complications develop and before the prognosis is hopeless. This statement is particularly applicable in children, as there is less fibrous tissue walling off the lesion, hence a more rapid progression of the disease results. If the first patient (case 1) had been treated surgically earlier, the outcome might have been more successful. Also, if the third patient (case 3) had been operated on sooner, it is possible that excision of the left lower lobe might have been feasible instead of complete extirpation of the lung. The second patient (case 2) is an example of one given early surgical treatment because of a rapidly spreading lesion, with apparent success.

5. (*a*) Bailey, C. P.: Lung Resection for Pulmonary Tuberculosis, J. Thoracic Surg. **16**:328, 1947. (*b*) Brewer, L. A.; Dolley, F. S., and Jones, W. M. G.: Indications for Pulmonary Resection for Tuberculosis by Lobectomy and Pneumonectomy, Dis. of Chest **14**:491, 1948.

6. Sellors, T. H.: Treatment of Pulmonary Tuberculosis in Children, Proc. Roy. Soc. Med. **37**:588, 1944. Maier, H. C.: Lobectomy and Pneumonectomy in Pulmonary Tuberculosis, Am. Rev. Tuberc. **58**:576, 1948. Cantonnet Blanch, P.; Roca Esteves, A., and Cantonnet Blanch, H.: Surgical Collapse Therapy: Results and Commentaries on Thoracoplasty in Children, Rev. de tuberc. d. Uruguay **5**:**718**, 1936.

7. Overholt, R. H., and Wilson, N. J.: Pulmonary Resection in the Treatment of Pulmonary Tuberculosis, J. Thoracic Surg. **14**:55, 1945.

Thus, the two most important indications in children are progressive unilateral disease and failure, or expected failure, of collapse therapy to arrest the pathologic invasion. In 3 of our patients the conditions fit the former indication and treatment apparently was successful. The first patient (case 1), whose condition went on to progression, had a lesion in the other lung. However, contralateral pathologic involvement may not necessarily rule out resectional surgical treatment. Brewer, Dolley and Jones [4b] stated that any lesion in the other lung should be quiescent for at least a year, but Gilbert [5] maintained that small, noncavitary lesions in the opposite lung are not a contraindication. Nevertheless, it probably would be wise to proceed cautiously with surgical intervention when such a lesion is present in children, because of the failure of the disease to stimulate production of fibrous tissue around the pathologic lesion.

There may be another indication in children, namely, the progressive primary complex. In this condition there is a rapid progression of the pathologic invasion, usually beginning in one lung and terminating fatally. It is difficult to diagnose, since the spread may stop at any time and spontaneous recovery occur. It is interesting to speculate that this condition may be arrested with excision of the diseased lung or lobe. In 1 patient (case 2), the course of the disease was extremely rapid, with caseation and liquefaction occurring early. A fatal termination, similar to that of her sibling a short time previously, seemed certain. Today she is free from symptoms, apparently well and attending public school on a full time basis.

The ultimate prognosis of these patients must be viewed from two aspects: (1) the status of the tuberculous lesion in the contralateral lung after operation and (2) the future cardiopulmonary reserve.

Whether a disease such as tuberculosis can be eradicated by surgical intervention is open to question. One main objection to pneumonectomy for pulmonary tuberculosis, now that the surgical mortality has been drastically reduced, is that tuberculosis is a systemic disease with seeding throughout the body and that surgical methods can remove only the largest and most acute lesions. That is the reason extreme care should be taken to rule out the presence of a cavitary lesion in the opposite lung. Tomography is indispensable, and surgical treatment should not be considered without serial roentgenograms first being taken.

Since there are no comparable series in children, a review of the results in adults is pertinent. Sweet [8] recorded a mortality of 38.8 per cent, with good results in 44 per cent. The first series of Overholt and Wilson [7] had a mortality of 38 per cent, with good results in 45 per cent.

8. Sweet, R. H.: Lobectomy and Pneumonectomy in the Treatment of Pulmonary Tuberculosis, J. Thoracic Surg. **15**:373, 1946.

A later series showed 17.5 per cent with mortality and 48 per cent with good results.[9] Gale, Dickie and Curreri[10] reported a mortality of 6.25 per cent, with good results in 83.75 per cent. Statistics at Sea View Hospital showed a mortality of approximately 15 per cent, and 77 per cent with negative sputums whose conditions were arrested. In the 4 patients presented here, there were 1 in whom treatment failed and 3 in whom treatment was apparently successful.

None of the three commonest complications of this type of surgical procedure in adults, namely, bronchopleural fistula, empyema and contralateral spread, were encountered in our patients. Operative lesions in children heal better and more quickly than those in adults. For this reason, bronchopleural fistula may not be as frequent a complication in younger patients. In the immediate postoperative period they are more alert and less sensitive to pain. They, therefore, cough more readily and evacuate the contralateral lung of all the secretions which spill over during the operation, lessening the chances of contralateral spread. This may have been the reason that no rales were heard in the contralateral lung in any of the 4 patients, a symptom not infrequently encountered in adults after the operation. In addition, the greater resistance to infection in children should reduce the incidence of empyema in comparison with adults.

A factor which may materially alter the prognosis in children, and which is only infrequently encountered in adults, is the lymph node component. This is present in both the primary and the adult types of pulmonary tuberculosis in children. In an autopsy study of patients with progressive primary tuberculosis in whom caseous nodes were present on the ipsilateral side, in all cases there was some caseation of the nodes on the contralateral side.[11] With removal of the main focus of the disease, however, regression and healing of the nodes on the other side may be expected, as that is the process elsewhere in the body. Removal of the more infected kidney has frequently provided a starting point for arrest of the infection in the remaining kidney.[12] It has also been observed in the wards of Sea View Hospital that arrest of tuberculosis of the spine has a beneficial effect on the pulmonary disease.

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9. Overholt, R. H.; Langer, L.; Szypulski, J. T., and Wilson, N. J.: Pulmonary Resection in the Treatment of Tuberculosis, J. Thoracic Surg. **15**:384, 1946.

10. Gale, J. W.; Dickie, H. A., and Curreri, A. R.: Pulmonary Resection in the Treatment of Tuberculosis, Am. Rev. Tuberc. **59**:10, 1949.

11. Auerbach, O.: The Progressive Primary Complex, Am. Rev. Tuberc. **37**:346, 1938.

12. Lowsley, O. S., and Kirwin, T. J.: Clinical Urology, Baltimore, Williams & Wilkins Company, 1940, vol. 2, p. 1509.

Except for the first patient (case 1), streptomycin and penicillin were given routinely before and after operation, and their use materially bettered the operative results.[13]

With the assumption of permanent arrest of the disease in these patients, a question arises of their future activity with only one lung. It is well known that in adults there may be distention and emphysema of the remaining lung. It has been postulated that it is this distention which aggravates a preexisting focus, causing contralateral activation. The process may be somewhat different in children. Experiments in growing animals revealed that a true hyperplasia of the remaining lung takes place, with the formation of new alveoli.[14] Also, the younger the animal at the time of operation, the less the impairment of the cardiopulmonary reserve.[15] In children in whom the lungs have been removed for conditions other than tuberculosis, similar changes have been observed, with the healthy lung subsequently filling the entire thoracic cavity. Thus, the policy of not performing thoracoplasty, routinely advised for adults, in children after pneumonectomy may be of value in allowing more space for the remaining lung to become hypertrophied.

Lester and Cournand and their associates[16] did respiratory studies on 4 children who had pneumonectomies for bronchiectasis. They ranged in age from 5 to 11 years at the time of operation. Follow-up studies up to ten years after operation revealed the patients to be well and leading normal lives, with apparently no limitation of physical activity. Results of tests done after heavy exercise showed a minimal reduction of breathing reserve and a definite unsaturation of the arterial blood, when compared with results in normal control subjects. It was also noted that the capacity of the pulmonary vessels was such that a several fold increase in blood flow may be accommodated by one lung

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14. Bairth, G.; Crawford, C., and Rudstrom, P.: Pulmonary Function After Pneumonectomy and Lobectomy, J. Thoracic Surg. **16**:492, 1947. Bremer, J. L.: The Fate of the Remaining Lung Tissue After Lobectomy or Pneumonectomy, ibid. **6**:336, 1937.

15. Carter, B. N.; Longacre, J. J., and Quill, L. McG.: A Study of the Changes in Cardiorespiratory Physiology Following Total Pneumonectomy in Young Developing Animals, J. Thoracic Surg. **7**:325, 1938.

16. Lester, C. W.; Cournand, A., and Riley, R. L.: Pulmonary Function After Pneumonectomy in Children, J. Thoracic Surg. **11**:529, 1942. Cournand, A.; Himmelstein, A.; Riley, R. L., and Lester, C. W.: A Follow-Up Study of the Cardiopulmonary Function in Four Young Individuals After Pneumonectomy, ibid. **16**:30, 1947.

with negligible pressure changes. In this series and in a larger one including adults the authors observed only one instance of pulmonary hypertension following pneumonectomy.[17]

Rienhof,[18] studying children with traumatic atrophy of the left lung, found that restitutional compensatory dilatation was complete and that the right lung almost completely filled the left thoracic cavity. He was unable to elicit evidence that such dilatation of the lung is harmful. His follow-up observations of twenty to thirty years demonstrated that living with one lung is not incompatible with at least three decades through a vigorous youth, a normal adolescence and the hard labor of adult life.

It is obvious that when lobectomy can be performed instead of total removal of the lung the prognosis from a functional standpoint would be much better.[19] Lobectomies performed in children for bronchiectasis have given excellent functional results.[20]

SUMMARY

Four cases in which pneumonectomy was performed in children from 3 to 13 years of age are presented. It is pointed out that children tolerate the surgical treatment and postoperative period well and are less prone to the complications which occur in adults.

Thoracoplasty is contraindicated in patients of the growing age period. Nonperformance of this procedure may be of value in children as it allows for hyperplasia of the remaining lung. Excisional surgical treatment of pulmonary tuberculosis in children and infants is advocated in cases in which it is indicated.

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17. Cournand, A., and Berry, F. B.: The Effect of Pneumonectomy upon Cardiopulmonary Function in Adult Patients, Ann. Surg. **116**:532, 1942.

18. Rienhof, W. F.: Intrathoracic Anatomical Readjustments Following Complete Ablation of One Lung, J. Thoracic Surg. **6**:254, 1937.

19. Maier, H. C., and Klopstock, R.: Lobectomy for Pulmonary Tuberculosis, J. Thoracic Surg. **14**:20, 1945.

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USE OF VISAMMIN IN TREATMENT OF WHOOPING COUGH

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AND
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IN SPITE of the large amount of clinical research on whooping cough, no curative treatment of the disease has yet been discovered. Special serum therapy, although definitely beneficial in the early stages, is less so as the disease progresses.[1] Sulfonamide compounds, as well as penicillin, have no influence on the progress of the disease, their value being mainly against secondary infections.[2] The use of streptomycin seems to be promising as far as can be judged from the results of observations in vitro and of experiments on rats, but its use in human subjects is still under trial.[3] The recently suggested high altitude treatment is also as yet in the stage of investigation.[4] The present day treatment of the disease, once it has reached the paroxysmal stage, is, therefore, mainly symptomatic.

The commonest and, until now, probably the most beneficial treatment consists, in addition to ordinary nursing care, in the administration of sedatives or antispasmodic drugs of the anticholinergic or of the adrenergic groups. Frequently, various combinations of these forms of medication are observed to be more effective. Use of sedative, as well as antispasmodic, drugs has many disadvantages, especially in young children, since medication has to be continued over a long period and since, in order to be effective, the drugs have to be administered in maximal, almost toxic, doses. When used for a long time, as for patients with whooping cough, the undesirable side effects of the

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Visammin is called Khellin in European chemical literature.

From the Pediatric Department and from the Physiological Laboratory, Kasr-el-Aini Medical Faculty.

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2. Kohn, J. L., and Fischer, A. E.: Management of Whooping Cough with Special Reference to Infants, Am. J. Dis. Child. **73**:663 (June) 1947.

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4. Cardovil, M.: J. de pediat. **8**:209, 1942. Lauener, P., and Maeder, E.: Schweiz. med. Wchnschr. **72**:89, 1942.

medicament become exceedingly troublesome and even dangerous. A considerable field is, therefore, still open for further investigation on the symptomatic treatment of whooping cough and on the use of new remedies.

The present communication deals with the results of our observations on the treatment of whooping cough with visammin (also known as khellin) a drug which has recently attracted considerable attention as an effective coronary vasodilator [5] and as an antispasmodic aid in bronchial asthma.[6] The experimental and clinical evidence shows that visammin can be safely used in human therapy and that it has no undesirable side effects, even on prolonged administration.[7] The average therapeutic dose of visammin used in angina pectoris and in bronchial asthma is known, so that we could proceed with our investigation from an already established foundation.[8]

The dose of visammin for the adult with bronchospasm has been established at 3 to 3.5 mg. per kilogram of body weight administered by intramuscular injections. We find that intramuscular administration of visammin, or in fact of many other drugs, is undesirable, especially in young children, since it may precipitate most unpleasant and severe paroxysms. We, therefore, decided to use visammin only by oral administration. In consequence, the dose was increased to 4.5 mg. and in some patients even to 7.5 mg., per day per kilogram of body weight. This dose was divided into three or four administrations. No other drugs were given to the patients treated with visammin.

In view of the fact that visammin is rapidly absorbed from the intestine and is eliminated or destroyed in the body extremely slowly,[9] we hoped to reach a sufficiently high concentration of the drug in the circulating blood to cause a decided and lasting bronchodilatation. Experiments on perfused lungs of guinea pigs showed that concentrations of visammin of about 1 microgram per cubic centimeter are effective.[10] In order to gain some information in regard to the concentration of

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5. Anrep, G. V., and Misrahy, G.: Gaz. Fac. Med., Cairo **13**:33, 1945. Kenawy, M. R., and Barsoum, G. S.: ibid. **13**:39, 1945.

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visammin in the blood of our patients, samples of blood were taken during the course of the treatment and their visammin content was estimated by the colorimetric or by the biologic method.[11]

MATERIAL AND METHOD

Preparation of Visammin Used.—A considerable number of pharmaceutic preparations containing visammin are at present available commercially. In the work described here we exclusively used the liquid extract of Ammi visnaga, sold under the name of ammicardine,* and prepared and standardized by the Alpha Laboratories, of Cairo, Egypt. Occasionally, the standardization was verified independently in our laboratory. The extract contained no other active substance. The bitter taste of the extract was improved by the addition of orange syrup and water, the necessary dose being then calculated for each child in cubic centimeters of the diluted extract.[12]

Observation of Patients and Interpretation of Results.—Each child was kept under constant supervision of trained personnel, day and night. In addition to the general observation of the patient, a constant record was kept of (1) the number of paroxysms in twenty-four hours, (2) the duration of each paroxysm and (3) the number of whoops in each paroxysm.

In order to assess the severity of each case, as well as the general run of the disease, we used a method, which, although entirely arbitrary, gave satisfactory results, especially for comparative purposes. It is obvious that the condition of the patient cannot be adequately described by a simple statement of the number of paroxysms per day, since each paroxysm may vary in duration, as well as in intensity. Mild paroxysms are accompanied with a small number of whoops or may even be free from whoops altogether. On the other hand, severe paroxysms are accompanied with many whoops and may be prolonged. In order to express the condition of the patient by a single comprehensive figure, we decided not to rely on simply recording the number of the paroxysms or on stating their duration and intensity (number of whoops) but on the numeric product of these three characteristics of the paroxysm. For simplicity, we used the number of the paroxysms per day, their average duration in minutes and the average number of whoops in each paroxysm. The figure arrived at by multiplying these three factors was called by us the "whooping cough index." It may be argued that the character of the paroxysms shows such wide variations even within a single day that no average figure could be reliable. However, experience revealed that even extreme fluctuations did not materially influence the results of the observations and that the whooping cough index, calculated as stated previously, gives a good indication of the progress of the disease.

Using the whooping cough index, we classified our patients into four groups: those with mild attacks, with an index of about 500 and below; those with moderate attacks, with an index between 500 and 1,000; those with severe attacks, whose index was above 1,000 and those with extremely severe attacks, with an index above 2,000. The highest index encountered before treatment was 9,600 and the lowest, 95. The total number of patients investigated was 22, of which 8 had mild, 6 moderate, 6 severe and 2 extremely severe attacks.

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11. Anrep, G. V.; Kenawy, M. R.; Barsoum, G. S., and Fahmy, A. R.: Gaz. Fac. Med., Cairo **14**:1, 1947.

12. The Alpha Laboratories, of Cairo, Egypt, placed a free supply of ammicardine* at our disposal.

RESULTS OF TREATMENT WITH VISAMMIN

For three to four days after his admission to the hospital, each patient was kept under observation, without any medicinal treatment, to establish the severity of his attack. Chart 1 shows the effect of treatment with visammin on patients with mild, severe and extremely severe

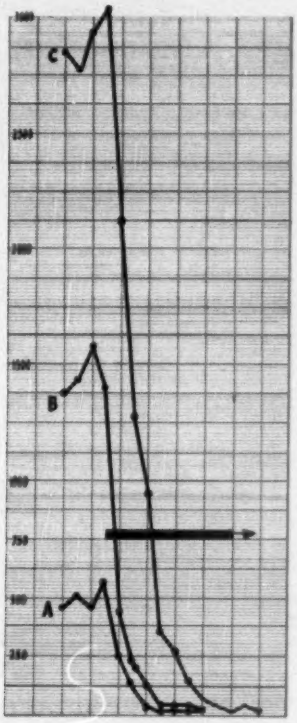

Chart 1.—Effect of treatment with visammin on whooping cough, as measured by the whooping cough index in a mild (*A*), severe (*B*) and an extremely severe (*C*) case. In this and the other figures, the whooping cough index is given on the ordinate and the duration of illness in days on the abscissa; the duration of treatment with visammin is shown by the heavy black line.

attacks. It may be seen that already on the first day of the treatment the index declined considerably. As would be expected, this decline was more rapid in those with mild cases.

In the patient with the exceptionally severe attack mentioned previously, whose maximal index was above 9,000, visammin was first

administered in a dose of 4.2 mg. per kilogram of body weight per day. This gradually brought about partial relief, the index declining in six days to about 4,500. The dose was then increased to 7 mg., which caused a drop of the index to about 750 on the first day of the treatment and to less than 100 on the following days (chart 2). The patient was an infant, 40 days old, weighing about 3,200 Gm. This patient was, however, not typical, since the disease was complicated with bronchopneu-

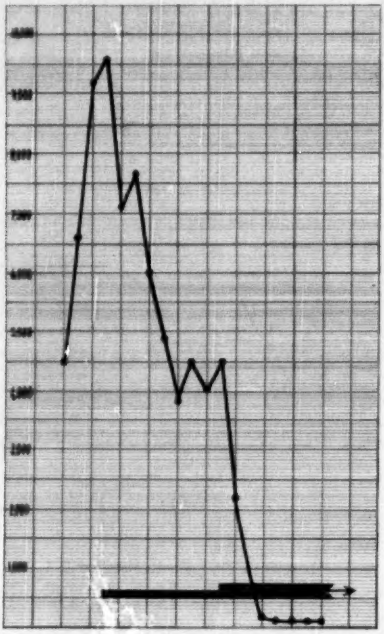

Chart 2.—Effect of treatment with visammin in an exceptionally severe case of whooping cough in an infant, 40 days old. The dose administered was at first 4 and then 7 mg. per kilogram of body weight per day.

monia, and he had to be treated with penicillin in addition to visamnin. Nevertheless, we believe that the life of the child was saved by the treatment with visammin.

Chart 3 shows the average results of treatment with visammin in 21 patients, the data on the aforementioned patient being excluded.

In some of the patients, for the sake of control, ammicardine® was administered after preliminary extraction with chloroform, which completely removed the active principle. Such administrations had no

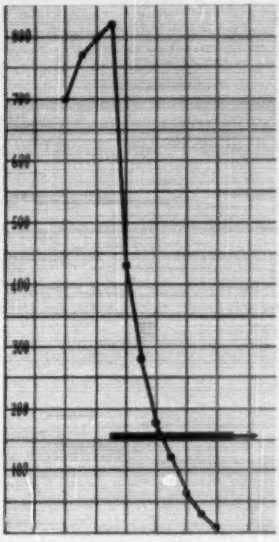

Chart 3.—Average results of treatment with visammin in 21 cases of whooping cough, as measured by the whooping cough index.

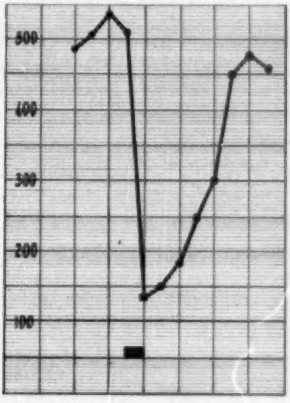

Chart 4.—Effect of administration of visammin for a single day on the whooping cough index in a patient with a mild attack.

beneficial effect whatever. In patients in whom the treatment with visammin was continued for only one or two days, the index temporarily declined, to rise again after a few days to the previous level (chart 4).

COMMENT

The experience gained as the result of treatment with visammin in a large number of patients with whooping cough shows that the amount of the drug administered is related to the improvement in the condition of the patient. Doses of less than 4 mg. per kilogram of body weight per day were either ineffective or effective only after a long delay. Doses of 5 to 7 mg. gave the best result. Higher doses have not yet been tried. It is obvious that with the increase in dose the concentration of the drug in the blood and tissues would also be increased. In order to

Visammin Concentration in Blood of Patients Receiving Various Amounts of the Drug

Group 1, 4 Mg. per Kg. per Day		Group 2, 6 Mg. per Kg. per Day		Group 3, 7.5 Mg. per Kg. per Day	
Number of Days from Beginning of Treatment					
4	8	4	8	4	8
0.7*	1.2	1.3	1.9	1.6	2.6
0.5	0.9	1.2	2.1	2.0	2.8
0.7	1.1	0.9	2.5	1.6	2.4
0.9	1.3	1.5	2.2	1.2	2.3
0.5	1.1	1.3	1.9	1.8	2.5

* Each pair of figures belongs to a different patient. The concentration is given in micrograms per cubic centimeter of blood.

determine the effective concentration of visammin in the blood, we collected samples of blood from three groups of 5 patients each, the first group receiving 4 mg. of visammin per kilogram of body weight per day for eight days, the second group 6.0 mg., and the third group 7.5 mg. It was observed that after administration of the first dose, the concentration of visammin in the blood rapidly rose to 1.5 to 2.4 micrograms per cubic centimeter but was not maintained at this level for more than a few hours. A steady concentration at about this level was reached after several administrations. The accompanying table shows the visammin level in the blood of our patients on the fourth and eighth days from the beginning of treatment with the drug. Each sample of blood was collected twelve hours after the last administration.

It can be concluded, as a result of these observations, that the effective concentration of visammin in the blood is between 1 and 2 micrograms per cubic centimeter.

This series of patients with whooping cough was not receiving any medicinal treatment other than visammin. It is, of course, obvious that administration of the drug together with small amounts of some sedative may possibly enhance the beneficial effect.

CONCLUSIONS

Visammin is a valuable drug in the symptomatic treatment of whooping cough. It is not dangerous and has no undesirable side effects, even in small children. The number of paroxysms and their intensity and duration are greatly and rapidly reduced by visammin. In consequence, the general condition of the patient, especially as regards sleep and appetite, improves.

It is recommended that visammin be administered orally in doses of 5 to 7 mg per kilogram of body weight per day, this dose to be divided into three or four administrations per day and continued throughout the paroxysmal stage of the disease. It is advisable to administer visammin in a syrup to mask its bitter taste.

A convenient method of following the progress of the disease and its treatment with the use of the whooping cough index is introduced.

DUODENAL ULCERS IN INFANTS

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PEPTIC ulcers in infants were described about one hundred and twenty years ago by Cruveilhier,[1] whose writings clearly illustrated 3 cases of gastric ulcers in infants, 1, 2 and 4 weeks old, respectively. It is commonly believed that this disease rarely occurs in infants and children. Therefore, its possibility has not received the consideration it justly deserves in cases of feeding difficulties, anemia, gastrointestinal disturbances and marasmus of obscure nature.

Judging from reports in the literature, it appears that the disease is commoner in the United States and on the European continent than it is in Great Britain. Paterson [2] stated that only 3 British cases had been reported prior to 1922 and that in the twenty years previous no case had been encountered at the Great Ormond Street Hospital, in London. As attention has been drawn to this condition, more and more cases are being recognized and reported. It nearly always makes its appearance after birth. Ladd and Gross [3] stated that it has been seen in stillborn infants, and Lee and Wells [4] reported a case of a gastric ulcer which perforated in utero. Bird, Limper and Mayer [5] made a thorough review of the cases reported up to 1941 in which operations were performed for peptic ulcers in infants and children. Guthrie [6] also recently reviewed the literature on this subject. She reported 9 cases of peptic ulcers observed at autopsy in the Glasgow Royal Hospital for Sick Children between 1914 and 1941, during which time 6,059 autopsies were performed on children under the age of 13 years. Those particularly interested in this subject are referred to these two excellent reviews.

From the Department of Pathology, Faculty of Medicine, University of Western Ontario and Meek Memorial Laboratory of Pathology, Victoria Hospital.

1. Cruveilhier, J.: Anatomie pathologique du corps humain, Paris, J.-B. Ballière, 1829, vol. 2, pt. 6.

2. Paterson, D.: Duodenal Ulcer in Infancy, Lancet **1**:63, 1922.

3. Ladd, W. E., and Gross, R. E.: The Abdominal Surgery of Infancy and Childhood, Philadelphia, W. B. Saunders Company, 1941.

4. Lee, W. E., and Wells, J. R.: Perforation in Utero of a Gastric Ulcer, Ann. Surg. **78**:36, 1923.

5. Bird, C. E.; Limper, M. A., and Mayer, J. M.: Surgery in Peptic Ulceration of Stomach and Duodenum in Infants and Children, Ann. Surg. **114**:526, 1941.

6. Guthrie, K.: Peptic Ulcer in Infancy and Childhood with a Review of the Literature, Arch. Dis. Childhood **17**:82, 1942.

ETIOLOGIC FACTORS

Most cases of peptic ulcers in infants occur without obvious cause. No significant cerebral lesions are observed. They may occur in the breast-fed infant, and no apparent sepsis is discovered. Many seemingly etiologic factors have been advanced from time to time. It has been suggested that overdistention of the stomach with large feedings may cause rupture of small vessels in the stomach, leading to digestion of the mucosa. This is a poor explanation; as will be pointed out later, gastric ulcers are rare in infants, while duodenal ulcers are much commoner. They usually occur on the posterior wall of the duodenum where food tends to stagnate. It has been said frequently that peptic ulcers are more apt to occur in the poorly nourished infant, but is it not more likely to be true that the ulcer is the cause of the malnutrition rather than the converse? Surely such factors as worry, mental strain, highly seasoned foods, alcohol and tobacco, commonly incriminated in the adult, must not be blamed for ulcers during infancy.

The matter of gastric acidity during early infancy deserves special consideration. This was carefully investigated by Miller.[7] He showed that the maximum acidity is usually reached within twenty-four hours of birth. Thereafter it falls during the first ten days and then gradually rises to the end of the first month, when it levels off. The most likely explanation for the initial fall in acidity is that a gastrogenic hormone is supplied through the placental circulation, the effect of which is transitory. With its disappearance, the infant is left to control its own gastric digestion on or about the tenth day of life. It has been observed many times that nearly all unfed infants have free acid in their gastric secretion at the time of birth. Investigations showed that the heavier the infant is at birth the more likely it is to have a more perfectly developed gastric mucosa and a more potent gastric secretion. In other words, the weight at the birth of the infant bears a close relationship to the amount of acid secreted by the stomach and to the degree of development of the gastric mucosa in the neonatal period.

REPORT OF CASES

Case 1.—This white male infant was admitted to the hospital at the age of 3 months because of anemia which did not respond to iron therapy. The infant was born at normal delivery, and the weight at birth was 7 pounds 7 ounces (3,374 Gm.). On his admission the weight was 9 pounds 2 ounces (4,139 Gm.). Transfusions were given and the infant was fed on special formulas, but one month later the weight had fallen to 8 pounds 12 ounces (3,969 Gm.). On September 12, three months after his admission to hospital, bright red blood was passed by bowel. One month later bouts of diarrhea occurred in which black stools were passed.

7. Miller, R. A.: Observations on the Gastric Acidity During the First Month of Life, Arch. Dis. Childhood **16**:22, 1941.

The hemoglobin concentration fell to 31 per cent. It was decided to submit the infant to surgical exploration, but he died an hour before the time set for operation.

Autopsy was performed one hour after death. The body was pale and emaciated. The principal feature was the presence of seven ulcers in the duodenum. All were situated on the posterior wall, three being proximal and four distal to the ampulla of Vater. Six were deep, penetrating, chronic ulcers and the seventh was superficial and acute (fig. 1). They varied from 4 mm. to 1.2 cm. in diameter. The distal part of the duodenum was drawn far over to the left and the base of ulcer 5

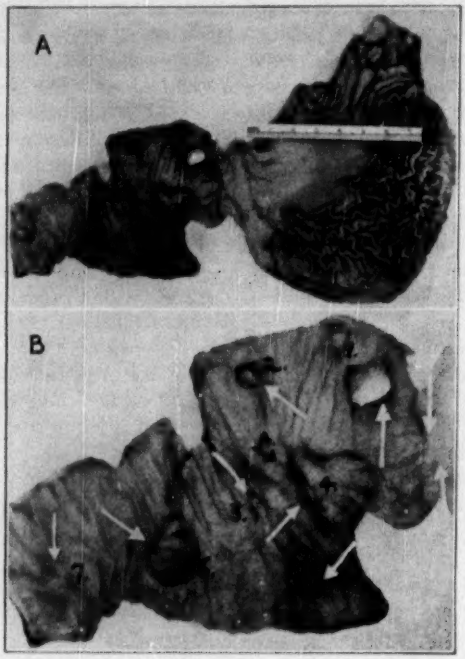

Fig. 1 (case 1).—*A*, stomach and duodenum showing seven duodenal ulcers. No ulcers are in the stomach. *B*, closeup view of duodenum. *A* indicates ampulla of Vater. Three of the ulcers are proximal and four are distal to the ampulla. Ulcer 7 is shallow and acute. The others are deep and penetrating. Ulcer 5 has perforated, producing localized peritonitis.

was adherent to the perirenal tissue over the upper pole of the left kidney by means of edematous fibroblastic inflammatory tissue. The coils of small intestine in this vicinity were bathed in a pale greenish yellow fluid which, on culture, yielded enterococci.

Case 2.—This patient was a male Indian infant, born at home at a normal delivery and admitted to hospital at the age of 3 weeks. The chief clinical signs were diarrhea since birth, frequent vomiting and blood in the stool on one occasion.

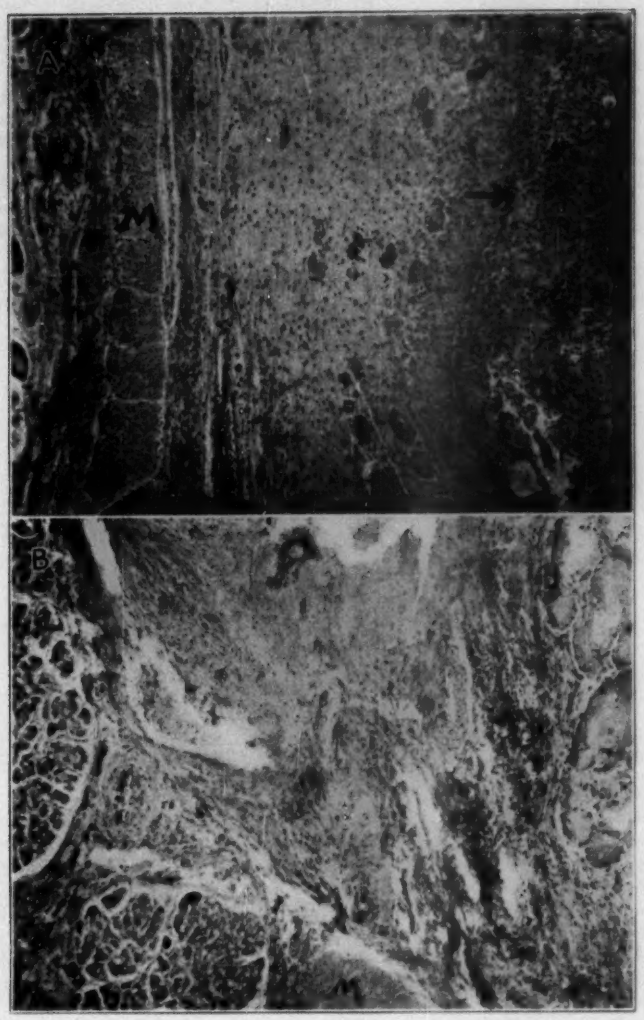

Fig. 2 (case 2).—*A*, photomicrograph showing a thick layer of inflammatory tissue in the subserous coat of the duodenum and a heavy layer of peritoneal exudate (× 120). *M* is the duodenal muscularis. The arrow indicates serosa layer of peritoneum. *B*, photomicrograph of ulcer eroding into pancreas (× 120). The wall of the duodenum is seen at the right, the surface of the ulcer at the top and the pancreas at the left. *M* indicates the duodenal muscularis, which ends abruptly in the base of the ulcer.

The stools remained loose and green and the infant became dehydrated. A transfusion was given. Terminally, the temperature was subnormal, the infant went into a state of collapse, with the development of a grayish blue appearance, and died on the twenty-fifth day after his admission to the hospital.

At autopsy the body weighed 2,300 Gm. and was greatly emaciated. The peritoneal cavity contained approximately 25 cc. of yellowish viscid fluid. Two ulcers were present in the duodenum, one on the anterior wall just beyond the pylorus with localized peritonitis over its base (fig. 2*A*) and the other just proximal to the ampulla, eroding the head of the pancreas (fig. 2*B*). The brain was examined and sections, especially of the hypothalamic area, revealed no lesions. One other finding of interest was suppurative appendicitis with localized peritonitis.

CASE 3.—This white male infant 3 months of age was admitted to the hospital because of difficulty in feeding and failure to gain weight satisfactorily. The

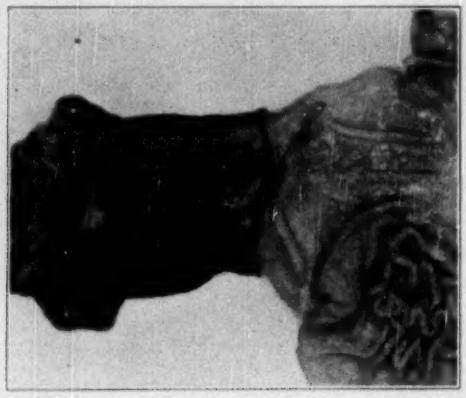

Fig. 3 (case 3).—Closeup view of gastroduodenal junction. Two ulcers are seen immediately distal to the pyloric ring. A prolongation of ulcer 2 shelves off longitudinally.

infant showed evidence of rickets, and during the first day in hospital he had two mild generalized twitching spells. The hemoglobin concentration was 56 per cent, with 2,860,000 red blood cells and 9,700 white blood cells. During the first ten days, considerable clinical improvement was noted, but the infant failed to gain weight. Then attacks of diarrhea and vomiting commenced. With a change in formula progress was satisfactory until the thirtieth day in the hospital, when the infant began passing loose yellow stools. From that time until death the diarrhea continued. Dehydration was combated with intravenous administration of fluids, and terminally dyspnea and cyanosis developed.

Autopsy revealed an emaciated infant, weighing 2,699 Gm. The peritoneal cavity showed nothing remarkable. In the duodenum immediately beyond the pylorus there were two deep, chronic ulcers. The smaller, 0.6 cm. in diameter, lay on the posterior wall. The other had a deep portion, measuring 0.8 by 0.4 cm., which shelved off distally into an elongated shallow ulcer (fig. 3). The ulcers had not

perforated. No definite bleeding point was seen. The mucosa surrounding these ulcers showed considerable edema and pallor, with a ring of congestion some distance away from the margins of the ulcers.

CASE 4.—This white male infant was admitted to the hospital at the age of 3 months. His birth was normal; he was full term and had been fed artificially since birth. Three days prior to his admission he began regurgitating and vomiting his feedings, and diarrhea commenced at the same time. The tentative clinical diagnosis was intestinal intoxication. Throughout his two week period of hospitalization his temperature was elevated, ranging from 100.2 to 103.4 F. Six days previous to his death the infant became grossly jaundiced; the abdomen was distended and the liver enlarged. Terminally a moderate degree of anasarca developed.

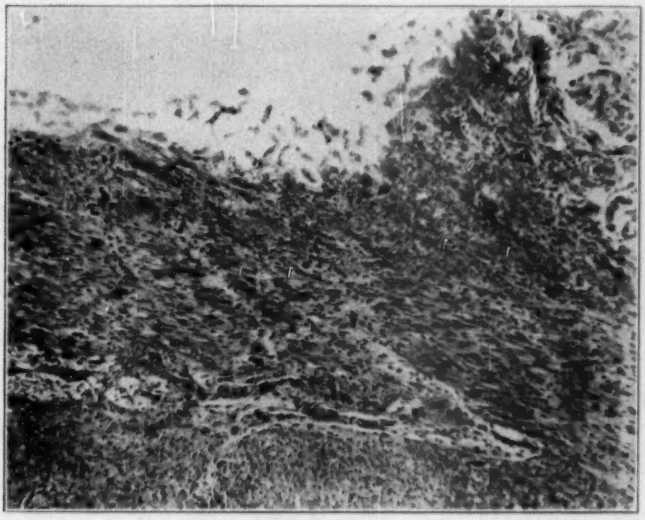

Fig. 4 (case 4).—Photomicrograph of ulcer (× 120). The ulcer is eroding down to intact muscularis, with slight fibrosis and mild inflammatory infiltration.

The hemoglobin concentration was 70 per cent and white blood cells numbered 12,050. He was treated with interstitial administration of fluids, protein milk feedings, a transfusion and penicillin intramuscularly.

Autopsy revealed an emaciated infant weighing 3,758 Gm. The body was deeply jaundiced. There was no evidence of ascites or peritonitis. The liver showed diffuse necrosis and extreme fatty degeneration. Both kidneys exhibited severe toxic nephrosis (fatty and albuminous degeneration). No lesions were seen in the large intestine. The mesenteric lymph nodes showed acute lymphadenitis. An ulcer, 1 cm. in diameter, was present on the posterior wall of the first part of the duodenum. It showed necrosis of the mucosa and submucosa and superficial involvement of the muscularis but had not perforated. Inflammatory cell infiltration was mild and slight fibrosis had occurred in the ulcer (fig. 4).

COMMENT

Since peptic ulcer was not suspected in any of the 4 cases here reported, no special clinical investigation was carried out. As a matter of fact, according to Moore [8] and Kennedy,[9] gastric analysis is an unreliable diagnostic aid in infants. Roentgenologic studies with a barium sulfate meal are difficult to conduct and are seldom made in infants.

In case 1, four of the ulcers were situated distal to the ampulla, a condition which is unusual. No good explanation for this has been found. Perhaps the acidity of the gastric secretion was unusually high

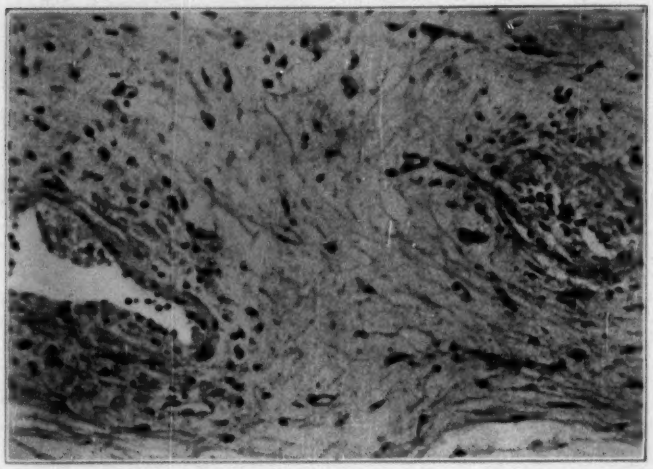

Fig. 5 (case 1).—Photomicrograph of ulcer 5 showing fibroblastic inflammatory tissue and endarteritis obliterans in base of ulcer (× 230).

and it was inadequately alkalized by the bile and pancreatic juice. No disease of the liver, biliary passages or pancreas was observed in this case.

The development of well defined zones, fibrosis, endarteritis obliterans and complete deficiency of the muscularis in the base of the ulcer, pathologic features characteristically seen in chronic peptic ulcers of adults, were observed in most of the ulcers in the cases here reported (fig. 5). Some were progressive, penetrating ulcers, and two had perforated but were walled off, producing only localized peritonitis. Inflammatory cell infiltration in the ulcers was relatively mild in all

8. Moore, O. M.: Peptic Ulcer in Children, Canad. M. A. J. **44**:462, 1941.
9. Kennedy, R. L. J.: Peptic Ulcer in Children, J. Pediat. **2**:641, 1933.

cases. Fibroblastic response varied from a mild to a pronounced degree.

All the ulcers in these 4 cases were duodenal. The preponderance of duodenal over gastric ulcers is shown in the numerous publications. Until 1942, only twenty-six chronic gastric ulcers had been reported in children under 12 years of age,[10] while during the same period well over three hundred duodenal ulcers were recorded.

In the 4 cases here reported the ulcers were multiple, except in case 4. Holt [11] stated that about two thirds of the ulcers in children are single and another author [6] remarked that ulcers are usually single but may be multiple.

In these cases it has not been possible to link any definite infection with the duodenal ulcers as causative factors. None included infection of the middle ear or demonstrable infection of the upper respiratory tract. Mild pneumonia was observed in 1 case at autopsy but it was considered a terminal condition.

The age incidence in my cases is considerably younger than in the majority reported in the literature. The oldest of these 4 infants was 8 months and the youngest 6 weeks of age at the time of death, while pediatric cases of duodenal ulcers usually occur in the childhood period (1 to 9 years of age or older).

SUMMARY

Four cases of duodenal ulcers are reported in infants, 8 months, 6 weeks, 4 months and 3½ months old, respectively, all of whom were boys.

In all 4 cases the ulcers were multiple and showed pathologic features of penetrating chronic ulcers, except for the ulcer in case 4 and one of those in case 1, which were of the acute type. In 2 of the cases ulcers had perforated, producing areas of localized peritonitis. In 1 ulcers occurred both distal and proximal to the ampulla of Vater, while in the other 3 the ulcers were proximal to the ampulla. In 1 case coexisting acute appendicitis was observed. No gastric ulcers were seen in these cases. No significant disease was observed elsewhere in the body, except wasting of the lymphoid tissue, albuminous degeneration of the liver and kidneys and, in case 4, fatty degeneration of the liver and hepatic necrosis. Mild pneumonia was present in 1 case.

10. Kraemer, M., and Townsend, L.: Chronic Gastric Ulcer in a Six Year Old Child, Am. J. Digest. Dis. **9**:338, 1942.

11. Holt, L. E.: Duodenal Ulcers in Infancy, Am. J. Dis. Child. **6**:381 (Dec.) 1913.

No apparent etiologic factors were discovered in the cases here reported. None of the infants was breast fed. All presented difficulties in feeding such as failure in gaining weight satisfactorily, anemia, vomiting, diarrhea and gradual marasmus. Blood was present in the stools in 2 of the cases. None was diagnosed correctly ante mortem and the ulcers were discovered for the first time at autopsy. It is suggested that peptic ulcer should be considered more frequently than in the past as a possible cause of such disease conditions.

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HYALURONIDASE IN ADMINISTRATION OF FLUIDS

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AND
JOHN E. FARLEY Jr., M.D.
PROVIDENCE, R. I.

THE PURPOSE of this paper is to establish further the usefulness of hyaluronidase, a relatively new agent in facilitating administration of fluids in pediatric practice, and to present results of numerous studies on toxicity performed to insure the relative safety of alidase,[®] [1] the commercial hyaluronidase product used in this clinical investigation.

Duran-Reynals [2] and McClean [3] were the first to note a spreading factor, hyaluronidase, present in testicular extract aiding spread of subcutaneously injected dye and fluid. This factor has since been obtained from many sources, including snake venom, leech, spider and bee extract, spermatozoa, some carcinomas and many bacteria. Chain and Duthie [4] identified the spreading factor as a mucolytic enzyme which acts on hyaluronic acid,[5] a mucopolysaccharide which in its native form is a gel or mucin clot not bound to protein.

By use of histochemical methods such as metachromic reactions of certain dyes, acid mucopolysaccharides are shown to be present within both epithelial and connective tissue, including cartilage, nucleus pulposus, Wharton's jelly, cornea, vitreous humor, synovial fluid and elastic fibers of blood vessels, and within the cytoplasm and in the secretions

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From the Department of Pediatrics, Charles V. Chapin Hospital, Dr. Harold G. Caulder, chief of pediatric service.

1. Alidase® is the trade name of the commercial hyaluronidase product which was supplied through the courtesy of Dr. Irwin C. Winter, director of clinical research, G. D. Searle & Co., Chicago 80.

2. Duran-Reynals, F.: Effect of Extracts of Certain Organs from Normal and Immunized Animals on Infecting Power of Vaccine Virus, J. Exper. Med. **50**: 327, 1929.

3. McClean, D.: The Influence of Testicular Extracts on Dermal Permeability and the Response of Vaccine Virus, J. Path. & Bact. **33**:1045, 1930.

4. Chain, E., and Duthie, E. S.: Identity of Hyaluronidase as Spreading Factor, Brit. J. Exper. Path. **21**:324, 1940.

5. Myers, K.; Smith, E. K., and Dawson, M. H.: Isolation of Mucopolysaccharides from Synovial Fluid, J. Biol. Chem. **128**:319, 1939. Myers, K.: Biological Significance of Hyaluronic Acid and Hyaluronidase, Physiol. Rev. **27**:335, 1947.

of the respiratory, gastrointestinal and genitourinary tracts. The chemical basis of the spreading reaction of hyaluronidase is the depolymerization of the hyaluronic acid gel by hydrolysis, thus reducing the high viscosity of hyaluronate gel and facilitating fluid diffusion. It is probable that faster absorption follows this greater diffusion, as the fluid is brought into contact with the surface area of more capillaries.

Hyaluronidase has been shown also to hydrolyze to a minimal degree another similar mucopolysaccharide, chondroitinsulfuric acid, present in the ground substance of body tissue.[6] This hydrolysis probably also facilitates fluid diffusion.

The potentialities of administration of fluids subcutaneously with hyaluronidase were first established by Sannella [7] and Hechter and his associates.[8] Recently, Schwartzman [9] and Burket and György [10] reported favorably on the use of hyaluronidase in hypodermoclysis in pediatrics, but with limited toxicity studies.

TOXICITY STUDIES

Toxicity studies were performed on 10 children who, at the time of investigation, were for all intents normal. Twenty-five viscosity units of hyaluronidase was given subcutaneously in the left thigh to 4 patients daily for seven days. Doses of 250 viscosity units of a more concentrated preparation of hyaluronidase were administered in the same manner to the other 6 patients for the same length of time. Blood chemistry studies consisted of determinations of blood uric acid levels, creatinine and carbon dioxide-combining power. Cephalin flocculation tests of hepatic function were performed. Complete urinalyses were done, and red blood cells, white blood cells and hemoglobin concentrations were surveyed. The bleeding, clotting and clot retraction times and the reaction to the tourniquet test were determined on all patients. Electrocardiograms were taken, and rash, fever and local and generalized reactions were noted.

The aforementioned studies were done on all patients on the day prior to the first administration of the drug and on the third and seventh days after its use was begun. Results of these tests are presented in table 1.

Because of the fact that hyaluronidase hydrolyzes not only hyaluronic acid but also chondroitinsulfuric acid, which is a constituent of the mast cells of Ehrlich, it was thought that the possible effect of hyaluronidase on the liberation of heparin should be investigated, also its action in the so-called heparinoid activity, as first

6. Myers, K.: The Mucopolysaccharides of the Interfibrillar Substance of the Mesenchyme (Preprinted Abstracts), read before the New York Academy of Sciences, Section of Biology, Dec. 4, 1948.

7. Sannella, L. S.: Effect of Testicular Extract on Distribution and Absorption of Subcutaneous Saline Solution, Yale J. Biol. & Med. **12**:433, 1940.

8. Hechter, O.; Dopkeen, S. K., and Yudell, M. M.: Clinical Use of Hyaluronidase in Hypodermoclysis, J. Pediat. **30**:645, 1947.

9. Schwartzman, J.: Hyaluronidase in Pediatrics, J. Pediat. **34**:559, 1949.

10. Burket, L. C., and György, P.: Clinical Observations on the Use of Hyaluronidase, Pediatrics **3**:56, 1949.

described by Allen and his co-workers.[11] This was accomplished by means of the heparin-protamine titrations, as modified by Mercer,[12] along with routine clotting studies. However, no changes in heparinoid activity or disturbance in clotting indexes were noted.

Blood uric acid levels and creatinine were investigated because of possible renal and/or metabolic deviations. No significant variations were observed. The results of determinations of carbon dioxide-combining power showed that there was no effect on acid-base balance. It was previously suspected that prolonged administration of hyaluronidase might cause hepatic dysfunction. Cephalin flocculation determinations failed to confirm this feeling. Serial electrocardiographic tracings were interpreted as being without toxic myocardial changes or interference in the conduction mechanism.

Investigation of red blood cells, white blood cells and hemoglobin concentrations revealed no changes, and complete urinalysis showed no peripheral manifestations of a deleterious action on renal function.

TABLE 1.—*Effect of Seven Daily Injections of Hyaluronidase*

	Average Values		
	Control	3d Day	7th Day
Uric acid, mg./100 cc.	3.1	2.9	2.9
Creatinine, mg./100 cc.	1.08	1.06	1.02
Carbon dioxide-combining power, volume percentage	59	60	56
Cephalin flocculation	0	0	0
Bleeding time, minutes	1.5	1.2	1.3
Coagulation time, minutes	4	3	3
Heparin-protamine titration, micrograms			
1 hour	140	140	140
3 hours	120	120	120
24 hours	100	100	100
Clot retraction and reaction to tourniquet test		No change	
Blood counts and urinalysis		No change	
Electrocardiograms		No change	
Local reactions		None	

There were no local reactions, with the exception of occasional transient erythema, and no fibrosis was observed in the area of injection. No elevation of temperature or rash was noted in any patient. The only concomitant disturbing occurrence with the administration was a recurrence of migratory polyarthritis and elevation of the erythrocyte sedimentation rate in a patient with rheumatic fever who had been convalescing for six weeks and whose condition had been considered quiescent. The importance of this occurrence is difficult to evaluate.

Skin tests were performed on 150 patients in all, with the use of 2.5 viscosity units of hyaluronidase in 0.2 cc. of isotonic sodium chloride solution intradermally. The only reactions noted were transient erythema in approximately one fourth of the patients and in all of them it subsided rapidly. There were no urticarious eruptions in our series.

11. Allen, J. G., and Jacobson, L. O.: Hyperheparinemia: Cause of Hemorrhagic Syndrome Associated with Total Body Exposure to Ionizing Radiation, Science **105**:388, 1947. Allen, J. G.; Bogardus, G.; Jacobson, L. O., and Spurr, C. L.: Some Observations on Bleeding Tendency in Thrombocytopenic Purpura, Ann. Int. Med. **27**:382, 1947.

12. Mercer, R. D.: Personal communications to the authors.

From the results of this investigation we concur with Schwartzman [9] and Burket and György [10] in their opinion that hyaluronidase, in this case alidase,* is relatively nontoxic and can be safely administered in hypodermoclyses.

*

METHOD OF ADMINISTRATION OF HYPODERMOCLYSES

Simultaneous bilateral hypodermoclyses to the thigh were administered to 100 infants and children. Selection of patients was made on the basis of degree of dehydration and severity of illness, regardless of diagnosis. The hypodermoclysis fluid used in all patients was 2.5 per cent glucose solution in 0.425 per cent saline solution. One thigh (treated thigh) received the glucose-saline solution with the addition of 25 viscosity units of hyaluronidase injected into the tubing before the start of hypodermoclysis, while the other thigh (control thigh) received plain glucose-saline solution. No. 20 bore, 1½ inch (3.8 cm.) needles were utilized for all procedures and carefully introduced into the subcutaneous tissue of the anterolateral aspect of the thigh. The hypodermoclysis flasks were placed approximately 30 inches (76 cm.) above the level of the patient. No clamps were used on the tubing to attempt to regulate the speed of flow. Fifty infants, weighing 8 to 20 pounds (3,629 to 9,072 Gm.), received 150 cc. of fluid in each thigh, and 50 children, weighing 20 to 30 pounds (9.1 to 13.6 Kg.), received 200 cc. of fluid in each thigh. Absorption times were recorded in minutes from the beginning to the completion of the drip hypodermoclysis.

COMMENT

From the summary of results presented in table 2, it is readily noted that hyaluronidase had a definite accelerating action on the administration of fluid by hypodermoclysis in 96 per cent of the patients of the series. In 50 infants receiving 150 cc. of fluid in each thigh, hyaluronidase decreased the average absorption time of the hypodermoclysis from 197 minutes in the control thigh to 56 minutes in the treated thigh, an average decrease of 141 minutes. In the 50 children receiving 200 cc. of fluid in each thigh, hyaluronidase decreased the average absorption time for the hypodermoclysis from 152 minutes in the control thigh to 47 minutes in the treated thigh, an average decrease of 105 minutes. This is equivalent to a decrease of 3.5 and 3.2 fold respectively in the administration time of the fluid due to the enzyme, hyaluronidase.

The time for absorption with the use of plain glucose-saline solution varied greatly, ranging from one to six hours. It is easily understood that any hypodermoclysis necessitating two to six hours for absorption is most impractical and of little immediate value to the patient. Administration of fluid by hypodermoclysis with and without the facilitation of hyaluronidase appears greatly affected by the size of the patient, the state of dehydration and, especially, the position of the needle and the texture of the subcutaneous tissue. Patients of the Negro race were noted to absorb fluids relatively poorly with and without the enzyme, and in 1 patient (case 33) no fluid could be administered during a six hour period.

TABLE 2.—*Comparison of time for Administration of Fluid by Hypodermoclysis With and Without Hyaluronidase*

Amount of Fluid Given on Each Side, 150 Cc. Weight of Patients, 8 to 20 Lb.	Time, Minutes		Amount of Fluid Given on Each Side, 200 Cc. Weight of Patients, 20 to 30 Lb.	Time, Minutes	
Case Number	Treated Thigh *	Control Thigh	Case Number	Treated Thigh	Control Thigh
1	61	273	51	82	400
2	47	70	52	45	120
3	22	160	53	30	70
4	45	125	54	50	75
5	55	175	55	30	155
6	95	285	56	53	65
7	25	160	57	65	240
8	20	203	58	28	185
9	22	70	59	50	210
10	40	255	60	60	185
11	35	55	61	70	360
12	65	125	62	20	50
13	49	302	63	30	240
14	57	72	64	35	95
15	63	360	65	31	63
16	55	30	66	53	180
17	25	120	67	60	320
18	120	245	68	27	240
19	50	300	69	30	118
20	45	165	70	58	205
21	75	70	71	84	42
22	40	120	72	60	65
23	60	500	73	37	300
24	140	310	74	25	55
25	75	112	75	62	110
26	33	180	76	35	105
27	35	250	77	47	67
28	50	180	78	155	320
29	80	150	79	48	235
30	15	120	80	40	240
31	33	125	81	40	150
32	107	320	82	25	130
33	..	...	83	45	135
34	60	300	84	75	300
35	120	480	85	60	180
36	32	140	86	20	160
37	53	170	87	27	57
38	35	250	88	12	44
39	70	320	89	19	75
40	70	95	90	53	120
41	45	135	91	70	180
42	120	480	92	30	120
43	55	200	93	60	90
44	60	150	94	45	70
45	50	80	95	20	80
46	30	110	96	40	80
47	50	100	97	50	150
48	40	130	98	60	120
49	60	105	99	90	170
50	70	300	100	90	180

* A solution of 2.5 per cent glucose in 0.425 per cent saline solution with 25 viscosity units of hyaluronidase was given the treated thigh. The same solution of glucose and saline solution was given the control thigh without addition of the enzyme.

The absorption sites receiving plain glucose-saline solution were firm and tense with much localized swelling, while the sites receiving fluid plus hyaluronidase exhibited less swelling of a diffuse and soft nature. No local reactions or exacerbations of infections elsewhere were noted.

The duration of the effect of the spreading factor of one dose of 25 viscosity units of hyaluronidase was found to be four days. This was determined by giving 5 infants the initial hypodermoclyses with both the control fluid and the fluid containing hyaluronidase and by repeating bilateral hypodermoclyses of plain fluid daily until both sides exhibited equal absorption times.

Increasing the dose of hyaluronidase from 25 to 250 viscosity units had little increased acceleration effect on administration of hypodermoclyses in 10 children weighing 20 to 30 pounds who received 200 cc. of glucose-saline fluid into each thigh. The average decrease in time for administration of fluid due to inclusion of 250 viscosity units of hyaluronidase was 108 minutes and was equivalent to a 3.3 fold difference.

As the evaluation of pain resulting from the hypodermoclyses was most unreliable in infants and children, 250 cc. hypodermoclyses of glucose-saline solution were administered with and without 250 viscosity units of hyaluronidase to 5 normal young adults. After the first five minutes, no pain or discomfort was noted in the site receiving fluid plus hyaluronidase, but definite pain and discomfort of moderate degree was experienced for the entire duration, and thirty minutes after the completion, of the plain hypodermoclysis. Three patients stated that the site receiving the enzyme felt not only painless but minimally numb during the administration of the fluid.

SUMMARY

In a series of 100 infants and children, times for administration of fluid by hypodermoclysis were recorded with and without the use of alidase,* a commercial hyaluronidase preparation. Hyaluronidase had a definite accelerative action on the administration of fluid in 96 per cent of the patients, causing an average decrease in time of hypodermoclysis of 123 minutes, equivalent to a 3.3 fold decrease.

Toxicity studies performed all gave negative results and no complicating reactions were noted in this series of 120 hypodermoclyses with hyaluronidase. No intradermal sensitivity was detected on skin testing in 150 persons.

Hyaluronidase is a highly efficacious agent in facilitating administration of fluid by hypodermoclysis.

Dr. Edward J. West, Dr. Edmund G. Anderson, Miss Etta Jane Falk and Miss Pearl Rytel cooperated in this study.

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CYSTIC CHANGE IN THE PANCREAS

Its Experimental Production

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IN 1945, an unusual change was observed in the pancreas of an infant who had died from dysentery associated with nutritional edema resulting from a diet lacking animal protein. The change consisted in cystic atrophy of a small part of the acinar tissue. Other parts of the excretory system and the islets seemed to have remained intact.

Reproduction of the change experimentally was attempted by the use of various deficient diets and toxic agents. Trials to induce the lesion by dietary means were successful.[1] However, chronic poisoning by small doses of carbon tetrachloride brought about regular production of this change in our series.

EXPERIMENTAL METHOD

Male albino rats of the same strain, ranging in weight from 160 to 190 Gm., were used. They were fed a well balanced stock diet, with a liberal supplement of water-soluble vitamins and cod liver oil with added vitamin A. The daily amount of neither food nor water was restricted.

On the basis of numerous previous experiments, 0.07 Gm. of carbon tetrachloride per each 100 Gm. of body weight was administered by subcutaneous injection to 28 rats every day. Two rats were killed by a blow every five days, the first 2 on the fifth, and the last 2 on the seventieth, day.

PATHOLOGIC OBSERVATIONS

Macroscopically, nothing abnormal could be detected in the pancreases; however, in some animals killed after the eighth week, the organ seemed harder and more fibrous than normally and than those of the other rats.

Microscopic examination[2] revealed nothing abnormal in the pancreases of the 4 rats which were killed on the fifth and tenth days of the experiment.

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1. Results of dietary experiments and the influence of diets on toxic lesions of the pancreas will be reported in other papers.

2. Prof. J. Baló assisted with microscopic diagnosis.

Cystic changes were present in every rat treated with carbon tetrachloride for more than twenty days. The lesion was confined to circumscribed areas with a diameter of 500 to 1,500 microns. Several such areas could be detected in every section and it seemed that the longer the exposure to the poison the more foci were formed.

Fig. 1.—Photomicrograph of pancreas of rat killed on fifteenth day. Note vacuoles and atrophy. Beginning of lumen formation is apparent in the acinus situated in the lower right corner. Hematoxylin and eosin stain; ×450.

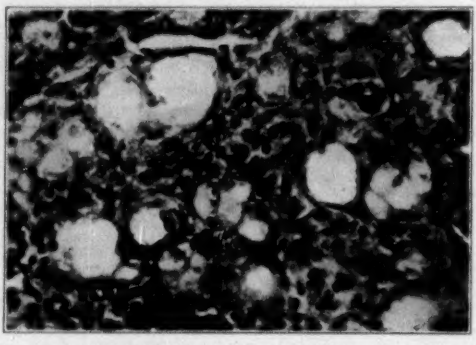

Fig. 2.—Photomicrograph of pancreas of rat killed on twenty-fifth day. Acinar structure is hardly recognizable except in the narrow strip of normal excretory tissue in lower right corner. Lumens are well established. Hematoxylin and eosin stain; × 300.

The earliest morphologic change detected was a complete disappearance of zymogen granules from certain areas, which then became eosinophilic. Then in the cytoplasm of the gland cells, around an acinus, first, vacuoles appeared; subsequently, the cells lost their spheroid shape and became endothelium-like, small and flat so that a lumen

was formed. As not all the cells of an acinus were equally involved in the process, the epithelium might be cuboidal on one side and quite flat on the other (fig. 1). With time, however, the epithelium everywhere became so low that wider lumens seemed to be lined with endothelium. Simultaneously, mast cells abundantly aggregated around the injured areas and fibroblasts appeared (fig. 2). The last stage recorded showed a number of widely dilated lumens embedded in a mass of con-

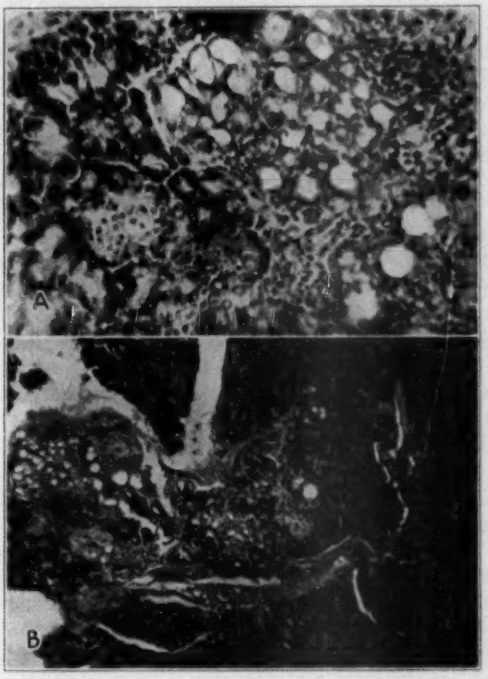

Fig. 3.—*A*, photomicrograph of pancreas of rat killed on fortieth day. A focus is present, consisting of numerous lumens surrounded by fibroblasts. A portion of normal tissue and an intact island of Langerhans appear on the right side. Hematoxylin and eosin; × 120. *B*, photomicrograph of pancreas of rat killed on sixty-fifth day. A shrunken lobule consisting of lumens embedded in connective tissue, several islands and blood vessels are seen. Hematoxylin and eosin; × 80.

nective tissue in which neither intercalated ducts nor any other parts of the normal excretory system were discernible except blood vessels (fig. 3).

In rats which had been treated for more than twenty days, all stages of the lesion were simultaneously present. Beginning cyst formation already appeared in animals killed on the fifteenth day (fig. 1).

Islands of Langerhans were always observed to be normal in the parts not affected, while they seemed somewhat increased in number and hypertrophied around the cystic changes.

In the lungs, various changes, such as infarcts, hemorrhages and emphysema, occurred but squamous metaplasia or other bronchial modifications were absent.

COMMENT

The lesion could be regarded as affecting differentially the exocrine system of the pancreas. Changes recorded in the number or size of the islands of Langerhans were interpreted as a consequence of the atrophy of the acinar tissue. It might be added that no sign of hyperinsulinism was recorded in the rats.

The picture described differed from the one observed following obstruction of ducts by metaplastic epithelium in subjects with vitamin A deficiency.[3] It must be repeated that the diet of the animals was by no means deficient in either vitamin A or any other known vitamin.

No regularity could be observed in the distribution of the affected areas, and they bore no relation whatever to the islands of Langerhans. There was no sign of the acini immediately surrounding the islands remaining intact.[4]

In order to exclude the possibility that the condition might be due to some dietary or infectious agent, 10 rats of the same strain were fed the same diet and kept together with the experimental ones. Nothing abnormal could be observed in the pancreases of the control animals.

In spite of the fact that no bronchial changes occurred in the rats and that the lesion produced was somewhat different from the cystic fibrosis of children, it would still be interesting to investigate the eventual connection of the two conditions; the more so as cystic changes similar to the ones reported here, together with fibrosis of the pancreas, can also be induced by dietary means. We were successful in producing fibrosis alone by various toxins. These studies will be reported on in another paper. In addition, further experiments will throw light on the fate of the changes described here and on the effect of carbon tetrachloride administered for more than seventy days.

SUMMARY

Production of cystic changes in the pancreas of rats by means of subcutaneous administration of carbon tetrachloride is described.

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3. Wolbach, S. B., and Howe, P. R.: J. Exper. Med. **42**:753, 1925.

4. Sergeyeva, M. A.: Anat. Rec. **71**:319, 1938. Selye, H., in Piersol, G. M., and Bortz, E. L.: The Cyclopedia of Medicine, Surgery and Specialties, Philadelphia, F. A. Davis Company, 1940, vol. 15, p. 15.

CARPAL AND EPIPHYSIAL DEVELOPMENT

Another Index of Nutritional Status of Rural School Children

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IN 1940, a study of the effectiveness of the school lunch in improving the nutritional status of the children in one rural school was begun, and in 1946 the first report was published.[1] During this study, special attention was given to skeletal development as shown by roentgenograms of the carpal bones and epiphyses of the distal portion of the radius and ulna. The report herein presented deals with carpal and epiphysial development as another index of the nutritional status of these children.

Ossification of these centers begins soon after birth and continues to maturity, thereby furnishing a continuous measure of skeletal progress. Moreover, the carpal bones and epiphyses are so easily evaluated by roentgenograms and have been used by so many investigators in the study of skeletal development that standards and norms are available for comparison.

While the worth of roentgenography in the study of pathogenic and traumatic conditions has been appreciated for years, the value of this method as a means of assessing nutritional status, which may affect the dates of appearance and degree of development of ossific centers in human beings, is just now being recognized. Pryor [2] reported that the order of ossification in the carpal bones of children was definite and fairly uniform in both sexes. When he noted differences in the rate of development of these centers, he suggested that ill health, accidents,

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1. Abbott, O. D.; Townsend, R. O.; French, R. B., and Ahmann, C. F.: Effectiveness of the School Lunch in Improving the Nutritional Status of School Children, Bulletin 426, University of Florida, Agricultural Experiment Station, 1946.

2. Pryor, J. W.: The Chronology and Order of Ossification of the Bones of the Human Carpus, Bull. Univ. Kentucky, 1908, vol. 1; Some Observations on the Ossification of the Bones of the Hand, ibid. 8:1, 1916.

disease, any interference with the blood supply or some modification of metabolism might cause delay or interruption of ossification.

Francis [3] pointed out that the orderly progress of ossification in individual children may be modified by illness, and he considered epiphysial ossification a more delicate objective indication of constitutional health than progress in height and weight.

Todd [4] was also of the opinion that the date of appearance and rate of development of the carpal bones, the growing ends of both the radius and the ulna and the shaft of the radius carried "evidence of health disturbances." Moreover, these disturbances left "marks that remained for some time." Because carpal centers are particularly sensitive to disorders in healths Todd considered them of little use as determinators of maturity, but apparently they could be of great value as indicators of nutritional health.

There are 84 ossific centers which appear at various times after birth. In well nourished children 67 of these centers appear in groups or sheaths during the first five years of life, while the remaining ones ossify within the next ten years, usually one at a time. There are 8 primary ossific centers in the wrist and in close proximity are the distal epiphyses of the ulna and radius. Francis and Werle [5] reported the time order of appearance of ossification in these centers in well nourished white male and female children in a favorable environment to be as follows:

	Boys		Girls	
	Year	Month	Year	Month
Capitate	..	2	..	2
Hamate	..	2	..	2
Triquetrum	..	10	..	10
Lunate	2	0	2	0
Greater multangular	4	2	2	8
Navicular	4	4	3	2
Lesser multangular	4	8	3	2
Distal part of radius	..	6	..	6
Distal part of ulna	6	2	4	6
Pisiform	10	4	7	2

The time order of ossification as given by Flory [6] differed in some particulars from the order of Francis and Werle but agreed in that by the age of 6 years seven carpal bones and the distal epiphysis of the

3. Francis, C. C.: Factors Influencing Appearance of Centers of Ossification During Early Childhood: II. A Comparative Study of Degree of Epiphysial Ossification in Infancy Under Varying Conditions of Diet and Health, Am. J. Dis. Child. **59**: 1006 (May) 1940.

4. Todd, T. W.: Atlas of Skeletal Maturation: I. The Hand, St. Louis, C. V. Mosby Company, 1938.

5. Francis, C. C., and Werle, P. P.: The Appearance of Centers of Ossification from Birth to Five Years, Am. J. Phys. Anthropol. **24**:273, 1939.

6. Flory, C. D.: Osseous Development in the Hand as an Index of Skeletal Development, Monograph of the Society for Research in Child Development, 1936, vol. 1, no. 3.

radius should be present in both boys and girls and the distal epiphysis of the ulna should be present in girls. According to Flory, these centers are so easily evaluated by roentgenograms that they can be used as an index of the development of other centers. This view appears justified, since several other investigators [7] have shown that ossification of the carpal centers is representative of the development of other centers due to appear at the same time. However, it does not follow that ossification of all centers in the sheath is necessarily progressing at the same rate. The observation does mean, however, that any factor, or factors, which causes retardation or advancement of one center may produce a similar effect on other centers.

MATERIAL AND METHODS

Location of the School and Selection of Subjects.—The location of the school and the prerequisites used in making a selection of subjects were described in the first report.[1] It may be said, however, that the cooperating school had an enrollment of approximately 200 pupils and was located in one of the poorer sections of the state. In this section fruit was scare, nutritional diseases of cattle endemic and milk production low.

The children came from an economically unstable class and, as shown previously, were grossly malnourished. At the beginning of the study in 1940, the prevalent defects were caries, diseased tonsils and disorders of nutritional origin: 90 per cent of the children had gingivitis; 71 per cent, anemia; 71 per cent, follicular conjunctivitis; 64 per cent, cheilosis and angular stomatitis, and 63 per cent, skeletal defects. Cardiac defects were observed in 22 per cent of the children. Because of association with anemia, these defects were classed with nutritional deficiency diseases. During the winters there was a high incidence of respiratory infections, associated with tonsillitis, sinusitis and otitis media. The obvious skeletal defects consisted primarily of round and stooped shoulders, winged scapulas and knock knee. Occasionally, a child showed spinal curvature.

Roentgenographic studies were not begun until September 1942. At that time the children had been served a well balanced noon meal for two school years (sixteen months). In addition to the noon meal, grossly malnourished children had been given midmorning and midafternoon lunches and preparations of iron and specific vitamins as indicated. As shown in the first report, great improvement in general health, physical status and developmental age had occurred.

Experimental Procedures.—From the 200 children enrolled in the rural school, the 162 children 6 to 13 years of age were the ones selected for the study of osseous development. The actual age of each child recorded in years and months was obtained from parents or from the school register.

Roentgenographic Technic: All roentgenograms were of the right hand and were made on high speed films in cardboard holders with a General Electric portable x-ray machine.

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7. Rotch, T. M.: Roentgen Ray Methods Applied to the Grading of Early Life, Phys. Ed. Rev. **15**:396, 1910. Sawtell, R. J.: How Children Grow: An Anthropometric Study of Private School Children from Two to Eight Years of Age, Studies in Child Welfare, Iowa City, University of Iowa Press, 1931, vol. 5, no. 1, p. 137. Baldwin, B. T.: Physical Growth of Children from Birth to Maturity, Iowa City, University of Iowa Press, 1921, chap. 7.

Measurement of Osseous Development: Todd[4] presented standards or representative roentgenograms of the right hand of boys and girls for successive age periods, which ranged from three months after birth to 16 years for girls and 19 years for boys. Accompanying these standards were detailed descriptions of successive changes most typical of each carpal bone. By comparison of the roentgenograms of the wrists of the children with Todd's standards and descriptive guides, each child in the present series was given a bone age or, as designated by Flory,[6] an inspectional age.

The degree of development of the wrists of each child was found by comparing the angulations of each carpal bone and the epiphysis of the distal part of the radius and ulna with those of the standards and descriptive guides specific for children of each age and sex. Each carpal bone and epiphysis was then classified as mature or immature in size and shape for the age and sex of the child or as missing.

TABLE 1.—*Retardation in Development of the Wrist of One Hundred and Sixty-Two Rural Children as Measured by Differences Between Chronologic and Carpal Ages*

Number of Subjects	Chronologic Age: Mean Yr.	Chronologic Age: Mean Mo.	Chronologic Age: Standard Deviation Mo.	Carpal Age: Mean Yr.	Carpal Age: Mean Mo.	Carpal Age: Standard Deviation Mo.	Retardation Yr.	Retardation Mo.
				Girls				
34	6	3	± 4	5	1	± 12	1	2
22	7	5	± 4	6	3	± 12	1	3
11	8	5	± 3	6	5	± 10	2	0
9	9	5	± 3	8	0	± 12	1	5
11	10	7	± 5	8	5	± 16	2	2
6	11	4	± 2	10	6	± 15	..	10
				Boys				
17	6	4	± 4	4	1	± 16	2	3
11	7	3	± 4	5	2	± 20	2	1
11	8	6	± 3	6	5	± 8	2	1
3	9	5	± 5	8	7	± 16	..	10
10	10	6	± 3	8	10	± 17	1	8
11	11	1	± 3	10	2	± 14	..	11
6	12	1	± 2	11	4	± 8	..	11

Variations in carpal development of girls and boys 6, 7 and 8 years of age were shown by arranging the roentgenograms of these children according to sex and age from the most mature to the most immature. The roentgenograms for each sex and age were then grouped as follows: (1) those at or above Todd's standard for sex and age and representing maximum carpal development; (2) those below the standard, but representing the average and (3) those greatly below the standard, representing minimum carpal development.

EXPERIMENTAL RESULTS

The average chronologic and carpal ages and the average retardation in carpal development of 162 rural children 6 to 13 years of age are given in table 1. The data show that retardation was greatest in the three youngest groups of boys and in the girls 8 and 10 years of age and least in the groups 11 and 12 years of age.

The degree of development of each carpal bone and the distal epiphyses of radius and ulna expressed as mature, immature, connoting

underdevelopment for age and sex, or missing is given in table 2 for girls and in table 3 for boys. With one exception, the degree of development of the three oldest carpal bones (capitate, hamate and triquetrum) for the various age groups of girls was in essential agreement. The exception was seen in girls 10 years of age, when 55 per cent of them showed immaturity of the triquetrum, as against 36 and 45 per cent for immaturity of the capitate and hamate, respectively. The highest percentages of carpal maturity were recorded in the oldest girls. But even here a third of them showed immaturity of carpal centers due to

TABLE 2.—*Variation in Development of Carpal Centers and Distal Epiphyses of Radius and Ulna of Ninety-Three Rural Girls*

Number of Subjects	34		22		11		9		11		6	
Age, in years	6 to 7		7 to 8		8 to 9		9 to 10		10 to 11		11 to 12	
Carpal bones												
Capitate	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Normal development	16	47	8	36	4	36	5	56	7	64	4	67
Immature	18	53	14	64	7	64	4	44	4	36	2	33
Hamate												
Normal development	16	47	8	36	4	36	5	56	6	55	4	67
Immature	18	53	14	64	7	64	4	44	5	45	2	33
Triquetrum												
Normal development	15	44	7	32	4	36	5	56	5	45	4	67
Immature	19	56	15	68	7	64	4	44	6	55	2	33
Lunate												
Normal development	12	35	11	50	4	36	5	56	4	36	3	50
Immature	22	65	11	50	7	64	4	44	7	64	3	50
Navicular												
Normal development	6	17	3	13	3	27	5	56	4	36	3	50
Immature	23	68	18	82	8	73	4	44	7	64	3	50
Missing	5	15	1	5	..	..	..	..	..	..	..	..
Greater multangular												
Normal development	16	47	5	23	3	27	5	56	3	27	4	67
Immature	14	41	15	68	8	73	4	44	8	73	2	33
Missing	4	12	2	9	..	..	..	..	..	..	..	..
Lesser multangular												
Normal development	16	47	6	27	3	27	5	56	6	55	6	100
Immature	17	50	15	68	8	73	4	44	5	45	0	..
Missing	1	3	1	5	..	..	..	..	..	..	..	..
Distal part of radius												
Normal development	20	59	20	91	3	27	5	56	6	55	2	33
Immature	14	41	2	9	8	73	4	44	5	45	4	67
Distal part of ulna												
Normal development	12	35	6	27	3	27	4	44	5	45	5	83
Immature	4	12	9	41	5	46	5	56	6	55	1	17
Missing	18	53	7	32	3	27	..	..	..	..	..	..

appear during the first year of life. For most age groups of boys the degree of development of the capitate and hamate was in agreement or varied slightly. The greatest variation was observed in the boys 10 years of age. In this group 80 per cent had a mature capitate, while only 40 per cent had a mature hamate. In all except the oldest group the percentages of boys showing immaturity of the triquetrum were high and varied from 60 to 82. It will be noted that this center was missing in 1 boy of the group 6 years of age. As was observed in the girls, the highest percentages of carpal maturity were found in the boys of the oldest group; here 83 per cent had normal development of these, the three oldest carpal bones.

The lunate occupies the central position in the time order of appearance, but in the data presented, variations both in the time of appearance and in the degree of development of this center were seen. The percentages of girls of all ages showing immaturity of the lunate varied from 44 to 65. In the boys, those 12 to 13 years of age had the lowest percentage of immaturity, 17 per cent, while in boys of all other age groups, the percentages varied from 55 to 73.

The greater multangular, navicular and lesser multangular, all due to ossify during the third year of life for girls and during the fourth for

TABLE 3.—*Variation in Development of Carpal Centers and Distal Epiphyses of Radius and Ulna of Sixty-Nine Rural Boys*

	17		11		11		3		10		11		6	
Number of Subjects														
Age, in years	6 to 7		7 to 8		8 to 9		9 to 10		10 to 11		11 to 12		12 to 13	
Carpal bones														
Capitate	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Normal	3	18	5	45	3	27	2	67	8	80	7	64	5	83
Immature	14	82	6	55	8	73	1	33	2	20	4	36	1	17
Hamate														
Normal	3	18	5	45	4	36	2	67	4	40	6	55	5	83
Immature	14	82	6	55	7	64	1	33	6	60	5	45	1	17
Triquetrum														
Normal	3	18	4	36	2	18	1	33	4	40	4	36	5	83
Immature	13	76	7	64	9	82	2	67	6	60	7	64	1	17
Missing	1	6	..	..	..	..	..	..	..	..	..	..	..	..
Lunate														
Normal	5	30	4	36	3	27	1	33	3	30	5	45	5	83
Immature	7	40	6	55	8	73	2	67	7	70	6	55	1	17
Missing	5	30	1	9	..	..	..	..	..	..	..	..	..	..
Navicular														
Normal	1	6	2	18	0	0	1	33	1	10	5	45	5	83
Immature	5	30	4	36	11	100	2	67	9	90	6	55	1	17
Missing	11	64	5	46	..	..	..	..	..	..	..	..	..	..
Greater multangular														
Normal	2	12	2	18	0	0	1	33	2	20	5	45	5	83
Immature	4	24	3	27	8	73	2	67	8	80	6	55	1	17
Missing	11	64	6	55	3	27	..	..	..	..	..	..	..	..
Lesser multangular														
Normal	2	12	4	36	0	0	1	33	3	30	5	45	5	83
Immature	3	18	2	18	8	73	2	67	7	70	6	55	1	17
Missing	12	70	5	46	3	27	..	..	..	..	..	..	..	..
Distal part of radius														
Normal	13	76	5	45	7	64	1	33	3	30	7	64	5	83
Immature	4	24	6	55	4	36	2	67	7	70	4	36	1	17
Distal part of ulna														
Normal	1	6	3	27	4	36	1	33	1	10	7	64	4	67
Immature	1	6	3	27	4	36	2	67	9	90	4	36	2	33
Missing	15	88	5	46	3	28	..	..	..	..	..	..	..	..

boys, showed great variation not only in development but also in time of appearance. These carpal centers were immature or missing in 53 to 87 per cent of the two youngest groups of girls and in 64 to 94 per cent of the boys of comparable ages. All these carpal bones were present in girls 8 years of age, though they were immature in 73 per cent of the subjects. In boys of comparable age, these carpal bones were missing or immature in 100 per cent of the group. Girls and boys 9 years of age showed considerable decrease in carpal immaturity, but in children of the next age group the percentages of immaturity were again high and varied from 45 to 73 for the girls and from 70 to 90 for the boys.

It is of interest that 33 per cent of the girls 11 to 12 years of age had an immature greater multangular and 50 per cent had an immature navicular, yet there was no immaturity in the lesser multangular, the last carpal bone to ossify.

The distal epiphysis of the radius, due to ossify at the sixth month of life, likewise showed wide variations in development. The highest percentages of immaturity of this center were observed in girls 8 and 11 years of age and in boys 9 and 10 years of age, while the lowest were

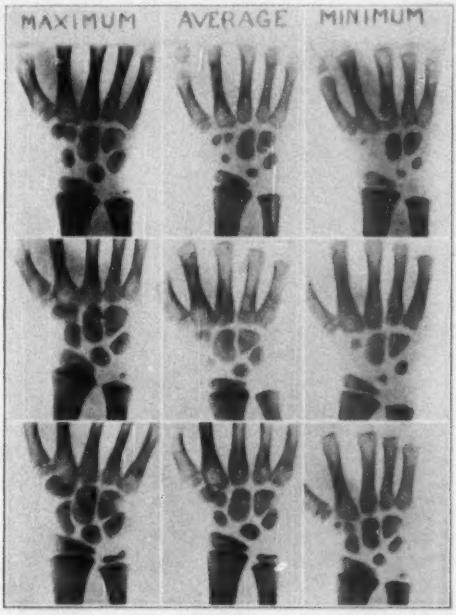

Fig. 1.—Variation in carpal development of girls 6 (top row), 7 (middle row) and 8 (bottom row) years of age.

seen in girls 7 years old and in the youngest and oldest groups of boys. In the children of all other age groups the percentages varied from 41 to 45 for the girls and from 36 to 55 for the boys.

The distal part of the ulna, due to ossify in girls during the fourth year of life and in boys during the sixth, showed much greater variation both in time of appearance and in rate of development than did the distal epiphysis of the radius. From the sixth to the ninth years, the percentages of girls with this center missing were 53, 32 and 27, while in the boys of comparable age the percentages were 88, 46 and 28,

respectively. By the ninth year this epiphysis was present in all subjects, though the percentages of immaturity remained high until the beginning of the eleventh year.

In figures 1 and 2, roentgenograms representing the maximum, average and minimum carpal development of girls and boys 6, 7 and 8 years of age are shown. It is evident that there is a wide variation in carpal development in both boys and girls of the same chronologic age. Particular attention is called to the number of missing and

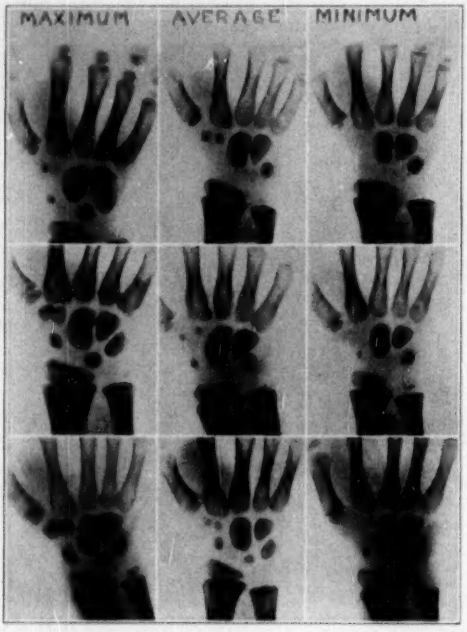

Fig. 2.—Variation in carpal development of boys 6 (top row), 7 (middle row) and 8 (bottom row) years of age.

immature carpal bones, and especially to the lunate, which is missing in the wrists of 3 boys and failed to appear in natural sequence in the wrists of 2 of them. The rating of all subjects of both sexes having maximum carpal development is in agreement with Todd's standards. Children with average development show some retardation, the girls 6 and 7 years of age about one year. On comparison of the carpal development of the girl of 8 years having average development with that of the girl 6 years old having maximum development, it is evident

that there are small differences. The differences, however, appear to be in favor of the girl 6 years of age, since angulations are somewhat more definite in the younger than in the older girl. The boys in the three age groups with average carpal development show greater retardation than do the girls of comparable ages. The roentgenograms representing minimum carpal development of the girls 6, 7 and 8 years of age show carpal development estimated as that of girls at 3¼, 3¾ and 5½ years, respectively. The carpal ages of the boys in these age groups were estimated as those of boys at 2¾, 3½ and 5¼ years, respectively. The least retardation, 2¾ years, was observed in the boy 8 years of age and the greatest, 3½ years, in the boy of 7 years.

The distal part of the radius appeared to be fairly well developed in all subjects of both sexes, but the distal part of the ulna was mature in only 1 subject, the girl 8 years of age with the greatest carpal development. In all other subjects, this epiphysis was missing or immature.

These roentgenograms show also the wide variations in carpal angulations in children of the same sex and age. Two of the earliest signs of maturity are the indentation on the radial side of the capitate and the closing up of the capitate to the hamate. These signs appear in well nourished children during the third and fourth years, respectively. The data showed that these signs were present only in girls with maximum carpal development and in boys 7 and 8 years of age in the same developmental grouping.

In figure 3, roentgenograms of the right hand of a boy made at the ages of 10, 11, 12 and 15 years, together with a brief history, illustrate how the carpal centers record the effects of malnutrition and, later, the effects of improved nutrition. When this boy was first examined, he was 9 years of age and, though suffering from gross malnutrition due to multiple deficiencies, showed no well defined signs of any one specific deficiency, unless it was that of iron and, perhaps, vitamin C. All the growth processes were retarded; height and weight had remained stationary or nearly so. He was 45½ inches (116 cm.) tall and weighed 37 pounds (16.8 Kg.). The hemoglobin concentration was low, 6 Gm. per hundred cubic centimeters of blood, but decreased pulse rate and decreased activity were compensations. He seldom played, had little emotional drive or endurance and had made no progress in school, as he had spent three years in the first grade. External skeletal defects were minor and consisted primarily of round and stooped shoulders and winged scapulas.

At the time the first roentgenogram was made, he had been given midmorning and midafternoon lunches and a well balanced noon meal, supplemented with iron and the indicated vitamins, for one and one-half school years (twelve months). He was now 10 years of age, but the roentgenogram showed only three carpal centers, capitate, hamate and

triquetrum, all due during the first year of life. While the effects of better food were not yet recorded by the carpal centers, they were seen in increases in height, weight and hemoglobin concentration and in his progress in school. At this time he was 47 inches (119 cm.) tall, weighed 45 pounds (20.4 Kg.), had a hemoglobin value of 10 Gm. and was out of the first grade.

When it was seen that several carpal centers were missing, he was given all the milk he could drink and extra vitamin D. It was evident

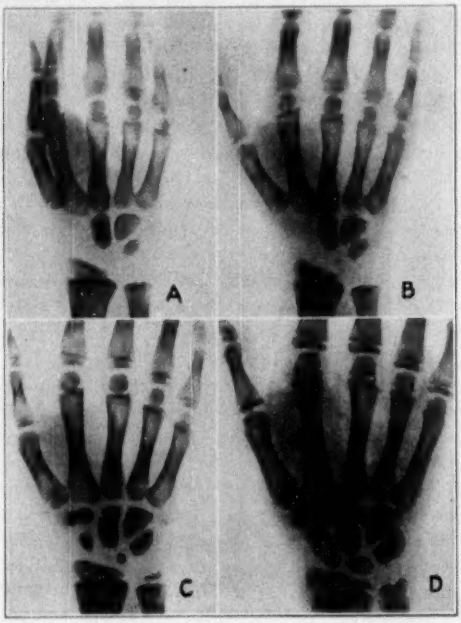

Fig. 3.—Successive roentgenograms of the right hand of a boy made at the ages of 10 (*A*), 11 (*B*), 12 (*C*) and 15 (*D*) years record the effects of malnutrition and, later, the effects of improved nutrition on carpal development.

that a reserve of bone building material was necessary if new carpal centers were to ossify. After another year on this regimen, a roentgenogram showed ossific centers or points for the navicular and lesser multangular, the last carpal bones due to ossify. However, the greater multangular and lunate bones, due earlier, were missing and the three carpal bones already ossified showed no angulations or signs of maturity.

At the end of the fourth year, the boy was 12 years old, 51 inches (130 cm.) tall and weighed 60 pounds (27.2 Kg.); the hemoglobin value

was 11 Gm. He was leading the fifth grade. The roentgenogram taken at this time showed 7 carpal centers, and, according to Todd's standards, he had a carpal development of a boy 6 years 9 months of age. A few angulations had developed, such as the overlapping of the greater and lesser multangulars, a formation of a process on the hamate, elongation of the capitate and formation of a distal dorsal peak on the lunate, the smallest and last carpal bone to ossify. On the other hand, some of the earliest signs of maturity, such as the indentation on the radial side of the capitate, the closing up of the hamate to the capitate and angulation of the capitate and hamate for metacarpals III, IV and V, had not yet appeared.

When the last roentgenogram was taken, he was 15 years old and was in the seventh grade. It will be noted that practically all the carpal bones had their adult shape and that the pisiform, though quite immature, was present. When compared with Todd's standards, the carpal development was that of a boy 12 years 3 months of age. Five years have now elapsed since the first roentgenogram was made. With an increase of five years in chronologic age, there has been an increase of 9 years 6 months in bone age.

COMMENT

Investigators of skeletal development have been concerned primarily with establishment of standards for the time of appearance of centers of ossification in healthy children. For this reason, the subjects were chosen from cooperative families among the economically stable classes. These subjects were free from gross mental or physical defects and had a favorable environment and an abundant and well balanced diet. Also, each child was under the active supervision of a physician, and any child who had a serious illness was excluded from the study. These standards, therefore, represent the development in children superior in physical and economic status.

The question naturally arises whether these standards should be used in assessing skeletal development or bone age of a group of previously malnourished children in an unstable socioeconomic group. According to Todd,[4] such a comparison is justified, since these standards are set up as a rule or measure of "quality, quantity or value" and, therefore, should be based on a relatively stable group. The carpus is a sensitive indicator of health disturbances, and standards should be based on its development in children of superior health status.

It is to be expected that individual variations will appear in skeletal development, as have been observed in other types of physical growth and development. However, it is generally accepted that the majority of children will fall into the average or near average group. Todd[4] stated that a child with a skeletal rating of twelve months or more below

his chronologic age has had a setback in development from which he has not yet recovered, even though he shows no signs of ill health.

The great differences between chronologic and carpal ages as observed in this study indicate that many of the children had had a major setback in ossification. It appears as though in these children growth had taken precedence over ossification for, while as reported earlier there were increases in height and weight,[1] roentgenograms showed that the effects of a well balanced meal and increased food consumption were not yet recorded by the carpal bones.

It is now recognized that there is a definite sequence, as well as date, of appearance, of centers of ossification in the carpal bones. The high percentages of missing and immature carpal centers reported herein show that both the sequence and the date of carpal appearance had been interrupted. The data also support the observation made by Francis and Werle [5] that when a carpal bone does not follow the orderly progress of ossification, the center for that bone is delayed until all other carpal centers are laid down. But, when the delayed center is finally ossified, angulations appear quickly. This is illustrated by the lunate shown in the third roentgenogram of the retarded boy (fig. 3). This carpal center, due during the third year of life, did not appear until the boy was 12 years of age. When it did appear, or was first noted, the distal dorsal peak was present and fairly well developed, even though the center was quite small. In a well nourished child, whose carpal development follows the schedule, the distal peak does not appear for several years after ossification of the center. There is the suggestion that this peak was laid down on the center. On the other hand, when angulations and other signs of maturity fail to follow the schedule, they, like the ossific center, are greatly delayed. The two signs often missing in this series were the indentation on the radial side of the capitate and the hamate closing up to the capitate. These signs of maturity should have been present during the third year of life but were still absent, for example, when the last roentgenograms were made of the retarded boy at 15 years of age, though signs due much later were present.

While many factors are involved in the process of ossification, the ones usually inhibiting or delaying the appearance of centers are inadequacies in vitamin D and in calcium and phosphorus intake. An adequate amount of vitamin D insures mineralization of the growing ends of the long bones and the ossification of centers, but it cannot provide the minerals. These must be present in the food.

Because of the slow rate of growth, the absence of signs of healed rickets and the fact that there was an abundance of sunshine and the children wore light clothing and played outdoors the year around, it seems evident that the intake of vitamin D was not a limiting factor.

It appears, therefore, that an inadequate supply of calcium and phosphorus was the primary cause of delayed ossification and development of centers. Milk is the best source of both calcium and phosphorus, yet in a preliminary study it was observed that 74 per cent of the children had no milk except a little used in coffee and in seasoning, while only a few of the remaining 26 per cent had a year around supply. MacNair and Roberts [8] reported that, when 1 pint (473 cc.) of milk was added to the regular diet of children living in an institution, the skeletal growth of these children, as measured by the Carter norm, increased one third of a year over the average to be expected. While it is possible to meet the recommended calcium intake of 1 Gm. per day without using milk, it is most difficult. From this study, it was concluded that retardation of ossification of carpal centers was closely related to the low consumption of milk.

SUMMARY

Data on the appearance and development of carpal bones and epiphyses of the distal part of the radius and ulna of 162 rural children 6 to 13 years of age are presented. The degree of skeletal development, or bone age, of these children was determined by comparing the roentgenograms of each child with Todd's standard and descriptive guide for carpal development according to sex and age.

The great difference between chronologic and carpal age as observed in many children indicates that these children had had a major setback in ossification. Wide variations in carpal age were seen in children of the same sex and age. Data on this group of children show that malnutrition interrupts both the sequence and the time of carpal appearance.

The successive roentgenograms of the greatly retarded boy illustrate the way in which the carpal centers record the effects of malnutrition and, later, the effects of improved nutrition.

The relationship of consumption of milk to skeletal development is pointed out.

CONCLUSION

Osseous development of the carpal bones and the epiphyses of the distal part of the radius and ulna offers another valuable means of assessing the nutritional status of school children.

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8. MacNair, V., and Roberts, L. J.: Effects of a Milk Supplement on the Physical Status of Institutional Children: II. Ossification of the Bones of the Wrist, Am. J. Dis. Child. **56:** 494 (Sept.) 1938.

BRONCHOPULMONARY GEOTRICHOSIS IN CHILDREN

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THE INCREASED interest in fungous diseases of the lung is attested by the large number of articles appearing in the literature during the past few years. This impetus apparently was initiated during World War II because of the numerous cases of benign coccidioidomycosis that developed in certain troop units. Smith [1] suggested that histoplasmosis also may occur endemically in a benign form. Subsequently, many surveys and studies were undertaken throughout the United States and the relationship of nontuberculous pulmonary calcifications to benign histoplasmosis has been established.

While studying coccidioidomycosis in the military service, one of us (R. H. K.) observed a case of bronchopulmonary mycosis which roentgenologically resembled tuberculosis and coccidioidomycosis, but which was proved to be caused by Geotrichum, a related fungus.[2] According to Dodge,[3] only 12 cases of Geotrichum infection had been reported by 1935, 8 of which were infections of the respiratory tract.

In 1933, Smith [4] reported 5 nonfatal infections due to Geotrichum and outlined the cultural characteristics necessary for identification of this fungus. In 1940, deAlmeida and DaSilva [5] isolated four strains of Geotrichum from the sputum of patients with pulmonary symptoms. The following year, Reeves [5] reported 79 cases of bronchopulmonary mycosis, only 1 of which was a Geotrichum infection. Recently, in a survey of 250,000 admissions to the hospital, Smith found 4 cases of geotrichosis among a total of 207 cases of fungous disease.[5] The impression that geotrichosis is a rare infection is probably incorrect. Undoubtedly, many cases have gone undiagnosed because of failure to culture

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Aided by a grant from the Committee on Scientific Research of the American Medical Association. Supported in part by the Michael Reese Research Foundation.

1. Smith, C. E.: Coccidioidomycosis, M. Clin. North America **27**:790, 1943.
2. Kunstadter, R. H.; Pendergrass, R. C., and Schubert, J. H.: Bronchopulmonary Geotrichosis, Am. J. M. Sc. **211**:583, 1946.
3. Cited by Kunstadter, Pendergrass and Schubert.[2]
4. Smith, D.: Oidiomycosis of the Lungs, J. Thoracic Surg. **3**:241, 1934.
5. Smith, D. T.: Pulmonary Mycosis, to be published.

the sputum of patients with chronic bronchial infections or atypical pneumonic infiltrations.

Recently, we completed a study on the incidence of mycotic infection of the lungs in children with acute respiratory disease.[6] During this study we observed a case of primary histoplasmosis in a Negro boy and followed the disease from its inception throughout the stage of pulmonary infiltration to beginning calcification. Histoplasma capsulatum was recovered from the blood and bronchial secretions.[7] Moreover, we observed 2 cases of active bronchopulmonary geotrichosis in a family who are residents of a farming community 40 miles (64 Km.) south of Chicago. We believe that the latter cases should be described because geotrichosis has not been reported previously in children to our knowledge. Furthermore, these cases serve to emphasize the fact that the diagnosis of mycotic disease of the lungs must be considered in bizarre pulmonary infiltrations, and that an etiologic diagnosis should be established, if possible, so that proper therapy may be instituted.

REPORT OF CASES

CASE 1.—R. Y., a white boy 6 years of age, became acutely ill with a sore throat, rhinitis and fever during the early part of June 1947. The acute symptoms subsided in a few days, but a low grade fever persisted. For this reason a roentgeno-

Fig. 1 (case 1).—Roentgenograms of the chest (*A*) taken on June 30, 1947, three weeks after onset of acute symptoms, showing soft, mottled-appearing infiltrations throughout both pulmonary fields and hilar adenopathy, and (*B*) taken on December 9, showing more extensive infiltrations and persistence of hilar adenopathy.

gram of the chest was taken on June 30, about three weeks after the onset of the acute symptoms, which showed mottled-appearing infiltrations in both lungs and prominent hilar adenopathy (fig. 1*A*). A provisional diagnosis of tuberculosis

6. Whitcomb, F. C.; Milzer, A., and Kunstadter, R. H.: Incidence of Mycotic Infections in Children with Acute Respiratory Disease, J. Pediat., to be published.

7. Kunstadter, R. H.; Milzer, A., and Whitcomb, F. C.: Primary Histoplasmosis with Recovery of Histoplasma Capsulatum from the Blood and Bronchial Secretions, J. Lab. & Clin. Med. **34**:1290, 1949.

was made, in spite of a negative reaction to the tuberculin test, and he was given a three weeks' course of treatment with streptomycin. However, he showed no improvement. The fever persisted, and during September he had a severe, productive cough. The sputum was whitish, mucoid and, at times, flaky in character but never tinged with blood. He lost considerable weight, became fatigued easily, complained of intermittent pains in the legs and spent much time in bed. On December 9, a roentgenogram of the chest revealed soft infiltrations throughout both lungs, more extensive than in the film made on June 30 (fig. 1). Administration of iodides was prescribed.

On December 15, he was admitted to Sarah Morris Hospital to the services of Dr. Julius H. Hess and one of us (R. H. K.) for observation. His temperature was 98.8 F. rectally; the pulse rate was 104, and respirations numbered 24 per minute. His weight was 35¼ pounds (16 Kg.). He coughed considerably and appeared pale, underweight and chronically ill. The tonsils were moderately enlarged and slightly reddened. Some dry crusts were present in both nostrils. There were

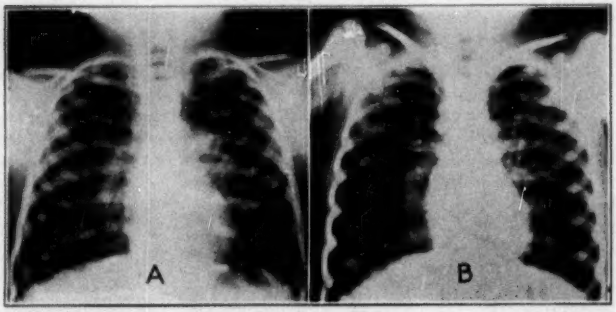

Fig. 2 (case 1).—Roentgenograms of the chest (*A*) taken on December 29, showing little change in the appearance of the infiltrative process in both pulmonary fields as compared with the picture on December 9, and (*B*) taken Jan. 20, 1948 one month after onset of iodide therapy, showing noticeable clearing of the pneumonic process in both lungs and a decrease in hilar adenopathy.

several carious teeth. The anterior and posterior cervical lymph nodes were slightly enlarged, discrete and nontender. The expansion of his chest was poor. Percussion revealed no significant findings. Musical rales were heard on inspiration over both lungs. There were no other significant findings. A roentgenogram of the chest taken on December 19 showed diffuse, mottled infiltrations throughout both lungs and hilar adenopathy still present (fig. 2*A*).

The essential laboratory findings are summarized in table 1. Nasopharyngeal smears and specimens of bronchial secretions obtained by bronchoscopic aspiration were cultured [8] and inoculated into animals. No tubercle bacilli or patho-

8. Fungous cultures were planted in duplicate on plates containing cystine brain heart infusion agar with 20 and 40 units of penicillin and streptomycin per cubic centimeter, respectively. One plate was incubated at 37 C. (98.6 F.) and the other at 25 C. (77 F.). Littman's potato dextrose and Sabouraud's mediums were also inoculated with each specimen and incubated at 25 C. Cultures for Actinomyces were made on beef infusion agar, using the spray dish technic.[6]

genic fungi were isolated. Cultures of samples of blood, stool and urine and of specimens obtained by gastric lavage were also negative for organisms. A summary of the results of fungous and tuberculin skin tests is shown in table 2. A positive reaction to Geotrichum antigen was obtained. The remainder of the tests gave negative reactions.

A diagnosis of pulmonary mycosis was made on the basis of the roentgenographic findings of persistent, soft, mottled-appearing infiltrations throughout both pulmonary fields, associated with hilar adenopathy, a whitish, mucoid and, at times, flaky sputum and a negative tuberculin reaction. The fact that all cultures were negative is not surprising because the patient had been given iodides continuously for two weeks prior to his admission to the hospital. We feel that the strongly positive cutaneous reaction to Geotrichum, which was also present

TABLE 1.—*Summary of Laboratory Findings in Case 1*

Date	12-16-47	1-9-48	1-12-48	3-30-48
Red blood cell count, millions	4.4	4.1	4.0	4.5
Hemoglobin concentration, Gm./100 cc.	11.5	10.5	11.0	11.5
White blood cell count	9,900	5,800	4,650	7,250
Differential count, percentage				
Neutrophils, segmented	65	78	66	58
Neutrophils, nonsegmented	6	6	3	4
Eosinophils	1	0	0	2
Basophils	6	1	0	0
Monocytes	1	7	3	5
Lymphocytes	21	8	28	31
Sedimentation rate (Landau), mm. per hour	30	32	16	9
Urinalysis	Negative	Negative	Negative	Negative
Blood chemistry				
Total serum protein, Gm./100 cc.	7.7	..	..	..
Albumin, Gm./100 cc.	4.4	..	..	..
Globulin, Gm./100 cc.	3.3	..	..	..

TABLE 2.—*Results of Fungous Skin Tests*

Patient	B. Y.	B. Y.	N. Y.	Mother	Father
Age, Years	6	4	2	24	25
Date	12-18-47	3-30-48	3-30-48	3-30-48	3-30-48
Skin Test Antigen *					
Tuberculin, 0.0001 mg.	0	0	0	0	0
Histoplasmin, 1:1,000	0	0	0	0	+++
Coccidioidin, 1:100 and 1:1,000	0	0	0	0	0
Blastomycin, 1:1,000	0	0	0	0	0
Torulin, 1:100	0	0	0	0	0
Geotrichum †	++++	+++	++	+++	++
Geotrichum control	0	0	0	0	0

* Histoplasmin and blastomycin were furnished through the courtesy of Dr. Arden Howell, of the United States Public Health Service; coccidioidin, through the courtesy of Dr. Charles H. Smith, of Stanford University, San Francisco; torulin (a filtrate of Cryptococcus neoformans) through the courtesy of Eli Lilly & Company, Indianapolis 6, and tuberculin (purified protein derivative), through the courtesy of the Tuberculin Institute of Chicago and Cook County, Ill.

† Geotrichum broth filtrate was diluted 1:10 and 1:100 with isotonic sodium chloride solution, while the geotrichum control was uninoculated broth filtrate in similar dilutions.

in the other members of the family, together with the negative response to the other fungous antigens, warranted the diagnosis of bronchopulmonary geotrichosis (table 2).

Furthermore, the clinical course and roentgenologic findings were similar to those in a proved case of a young adult reported by one of us (R. H. K.) recently.[8] Because of the excellent results obtained by the use of large doses of iodides in the previously reported case, this patient was treated similarly. He was given increasing doses of a saturated solution of potassium iodide U. S. P. by mouth, starting with 5 drops three times daily, increasing 1 drop daily to a maximum of 10 drops three times daily, and sodium iodide U. S. P., 3 grains (0.19 Gm.) daily, intravenously for a total of twenty-three consecutive injections from Dec. 12, 1947 to Jan. 11, 1948. During the first two weeks of iodide therapy, the cough became more productive and moist rales were heard throughout both pulmonary fields. Subsequently, the cough gradually subsided; the temperature became normal, and the abnormal physical signs in the chest disappeared. Intravenous administration of iodide was discontinued on January 11, twenty-three days after initiation of treatment because of fever and a cutaneous eruption due to the iodide. The fever subsided in forty-eight hours, and the rash disappeared in one week. In an attempt to accelerate the clearing of the pulmonary infiltrations, both lungs were given roentgen therapy.[9] A roentgenogram of the chest taken on January 20 showed notable clearing of the infiltrations in both pulmonary fields (fig. *2B*) and a decrease in hilar adenopathy. The boy was discharged from the hospital on January 31, greatly improved, with instructions to continue the administration of postassium iodide, 5 drops three times daily.

He was seen again on March 30. At that time he felt well; his appetite was good, and he had gained 4½ pounds (2 Kg.) since leaving the hospital. He had no cough. A roentgenogram of the chest still showed infiltrations in both pulmonary fields, apparently more focalized and less prominent compared with the film taken on January 20. Hilar adenopathy was still present (fig. 3*A*). He had been given potassium iodide continuously and his parents were instructed to continue this therapy. He was last seen on September 14 a little over a year after the onset of his infection. A tonsillectomy and circumcision were performed on September 1, with no complications. He felt well, his appetite was good and he was not coughing. He had been given potassium iodide continuously. A roentgenogram of the chest showed little change in the appearance of the focal lesions in both lungs as compared with the picture on March 30. There was still much hilar adenopathy (fig. 3*B*). Iodide therapy was discontinued.

Case 2.—B. Y., the 4 year old sister of R. Y., had mild acute symptoms of infection of the upper respiratory tract, with a fever lasting for a period of only two or three days, shortly after her brother became ill. A roentgenogram of the chest was taken on June 30, 1947 because of the pathologic changes noted on her

9. Radiation therapy was undertaken by Dr. Eric Uhlmann, director of the Tumor Clinic of Michael Reese Hospital. The patient received four treatments to the right anterior wall of the chest on Jan. 3, 5, 6 and 7, 1948. Three treatments were given to the left anterior wall of the chest on January 21, 22 and 23 and two to the right posterior wall of the chest on January 24 and 26. At each treatment a field of 10 by 15 cm. was irradiated at a distance of 50 cm., and the patient received 75 r on each occasion. The technical factors were 200 kilovolts constant potential, with 1 mm. of copper plus 0.5 mm. of aluminum filtration. The total amounts given were 300 r to the anterior wall of the chest, 225 r to the left anterior wall of the chest and 150 r to the right posterior wall of the chest.

brother's film. Slight enlargement of the hilar lymph nodes was present, but the pulmonary fields appeared clear. She remained free from symptoms. However, a roentgenogram of her chest taken on Feb. 4, 1948 showed pronounced hilar adenopathy and diffuse patchy infiltrations extending out from both hilar regions, involving principally the lower lobes (fig. 4*A*). On February 11, while at home, treatment was started with saturated solution of potassium iodide, 5 drops three times daily. She was seen by us for the first time on March 30, at which time

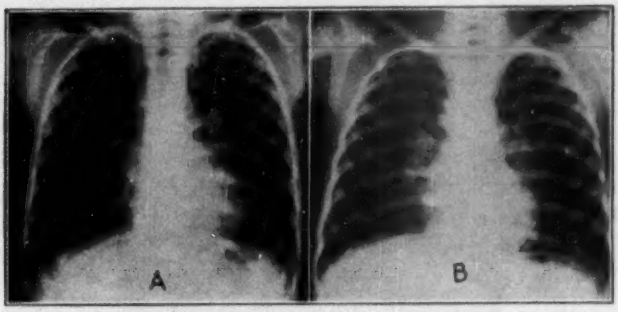

Fig. 3 (case 1).—Roentgenograms of the chest (*A*) taken March 30, showing increased focalization of the infiltrations in both pulmonary fields with persistence of hilar adenopathy, and (*B*) taken September 14, showing presence of small, irregular and nodular-appearing lesions in both lungs, with little change as compared with the picture of March 30. There is still much hilar adenopathy.

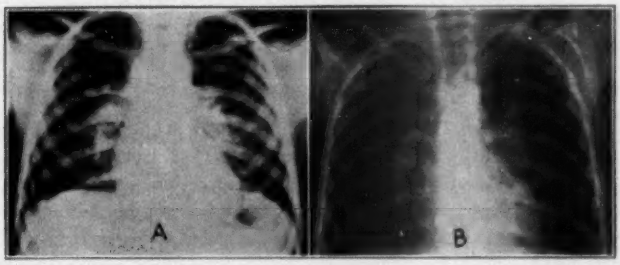

Fig. 4 (case 2).—Roentgenograms of the chest (*A*) taken Feb. 4, 1948 showing patchy infiltrations in both lungs fanning out from the hilar regions, with prominent hilar adenopathy, and (*B*) taken March 30, six weeks after onset of iodide therapy, showing clearing of the pneumonic process in both lungs, with persistence of hilar adenopathy.

she appeared perfectly well. A roentgenogram of the chest revealed hilar adenopathy and clearing of the pulmonary infiltrations (fig. 4*B*). Nasopharyngeal cultures yielded no fungi. The blood count was normal; the sedimentation rate was 4 mm. per hour (Landau method), and the skin test for geotrichosis resulted in a positive reaction (table 2). She was last seen on September 14. She had

been given potassium iodide continuously. She was perfectly well, and a roentgenogram of the chest showed clear pulmonary fields and a decrease in the hilar adenopathy (fig. 5). Iodide therapy was discontinued.

Other Members of Family.—A 2 year old sibling was entirely well. Serial roentgenograms of the chest showed hilar adenopathy but no evidence of pulmonary disease. The cutaneous reaction to Geotrichum was positive; all other skin tests gave negative reactions (table 2).

Both parents were in excellent health. The mother's chest film showed nothing abnormal. The father's roentgenogram showed small areas of calcification in the left pulmonary field and hilar region. Both parents had positive reactions to Geotrichum skin tests. The father gave a positive reaction to histoplasmin and a negative reaction to tuberculin.

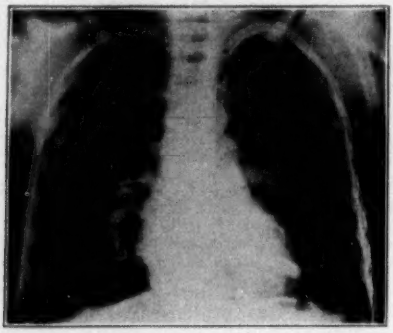

Fig. 5 (case 2).—Roentgenogram of the chest taken September 14, showing continuing clearness of the pulmonary fields with a decrease in the hilar adenopathy.

COMMENT

All 5 members of one family, 3 children and their parents, reacted positively to the Geotrichum skin test. The 2 older children, 6 and 4 years of age, respectively, showed evidence of active mycotic disease at approximately the same time. Their symptoms consisted of malaise, sore throat, cough and fever and the development of parenchymal infiltrates which appeared as soft, mottled areas throughout both pulmonary fields roentgenographically. Furthermore, hilar adenopathy was prominent in both children. The pulmonary lesions persisted for months and responded slowly to iodide therapy. In addition, the oldest child received roentgen therapy to both lungs. The younger of the 2 children had a milder infection, with fever of short duration and a slight nonproductive cough. The pulmonary lesions were less severe. In both children, hilar adenopathy diminished more slowly than the parenchymal infiltrations and in the second child was still present after complete clearing of the pulmonary fields.

The oldest child (case 1) had a productive cough with whitish and, at times, flaky sputum characteristic of Geotrichum infection.[4] Geotrichum was not recovered from the sputum or bronchial secretions of this child by culture or animal inoculation, probably because of previous iodide therapy. It was felt, however, that the diagnosis of bronchopulmonary geotrichosis was justified on the basis of the clinical course, including the characteristic sputum, roentgenologic findings of soft, mottled-appearing infiltrate throughout both pulmonary fields, with hilar adenopathy, and positive reaction to the Geotrichum skin test, with negative reactions to tuberculin, coccidioidin and histoplasmin. Furthermore, these cases were similar clinically and roentgenologically to a proved case described recently by one of us.[2]

The youngest child, 2 years of age, and both parents showed no evidence of pulmonary disease, although all reacted positively to the Geotrichum skin test. Apparently, the initial infection was extremely mild. In addition, the father had a positive reaction to histoplasmin, and possibly the small areas of calcification noted in his left pulmonary field and hilar regions in the presence of a negative tuberculin reaction can be explained on the basis of healed histoplasmosis and/or geotrichosis.

According to Dodge,[3] Geotrichum is a genus of the Eremascaceae imperfectae family and was first described by Link in 1809. In many respects it resembles Blastomyces dermatitidis and Coccidioides immitis. The organism has frequently been confused with the more pathogenic Blastomyces dermatitidis.[3] The genus Geotrichum is quite large and consists chiefly of saprophytic species. The fungus may produce infection of the skin and mucous membranes or of the lungs simulating chronic pulmonary tuberculosis. Thin-walled cavities may develop or, as in our cases, the infiltrates may appear as soft, mottled or irregular patchy areas scattered throughout both pulmonary fields and resembling coccidioidomycosis, moniliasis, North American blastomycosis, cryptococcosis [10] and histoplasmosis. The lesions are not characteristic of any specific type of pulmonary mycosis. A chronic bronchitis, with peribronchial thickening and without parenchymal infiltrates, may be present in some cases.[2] Hilar adenopathy is present and may persist for a considerable length of time after the pulmonary lesions have resolved.

The constitutional symptoms usually are not severe in proportion to the degree of pulmonary involvement. Cough, low grade fever and anorexia are usually present. Smith [4] emphasized that patients with clinical symptoms of chronic bronchitis or pulmonary tuberculosis, who have white, mucoid sputum containing grayish flakes, should be suspected

10. Smith, D. T.: Fungus Diseases of the Lungs: American Lectures in Chest Diseases, Springfield, Ill., Charles C Thomas, Publisher, 1947, p. 19.

of having an infection with Geotrichum. The organisms can be cultured from the sputum on Sabouraud's medium and identified by the rectangular arthrospores.

SUMMARY AND CONCLUSIONS

The clinical course and roentgenologic appearance of bronchopulmonary geotrichosis in 2 children, aged 6 and 4 years, respectively, are described. A 2 year old sibling and both parents also reacted positively to the Geotrichum skin test but showed no evidence of pulmonary disease. The father gave a positive reaction to histoplasmin and a negative reaction to tuberculin; a roentgenogram of his chest revealed multiple calcified areas in the left lung and hilar region which probably represented the healed stage of histoplasmosis and/or geotrichosis. Iodide therapy and roentgen irradiation (case 1) resulted in gradual improvement of the oldest child over a period of nine months. Iodide therapy alone resulted in a more rapid and complete clearing of the pneumonic process in the younger child (case 2) during seven months of observation.

Bronchopulmonary mycosis should be considered in the differential diagnosis of chronic bronchitis, atypical pneumonia, bacterial pneumonia, particularly the slowly resolving type, pulmonary fibrosis and tuberculosis. Geotrichosis must be differentiated from other mycoses, such as moniliasis, North American blastomycosis, cryptococcosis, coccidioidomycosis and histoplasmosis. An attempt to establish an etiologic diagnosis should be made by the use of all available diagnostic facilities, including history, serial roentgenograms, fungous skin tests, and cultures of sputum and bronchial secretions on Sabouraud's medium.

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FIBROSIS OF THE PANCREAS

Enterogastrone and the "Duodenal Mechanism" in Relation to Increased Appetite

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THE FOLLOWING studies on patients with fibrosis of the pancreas were carried out for two purposes: (1) to discover, if possible, an acceptable physiologic explanation for the ravenous appetite of these patients and its abatement with the administration of dried pancreas [1] and (2) to determine whether the pancreas is or is not involved in the production of an enterogastrone-like substance which might play a role in the "duodenal mechanism" of Gershon-Cohen.[2]

That orally ingested fat remains longer in the stomach than other foods has been long recognized.[3] That, furthermore, gastric motility [4] and gastric secretion [5] are decreased following its administration has also

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1. May, C. D., and Lowe, C. U.: Treatment of Fibrosis of the Pancreas in Infants and Children, Pediatrics **1**:159, 1948.

2. Gershon-Cohen, J.: A Duodenal Mechanism Regulating the Motor and Secretory Activity of the Stomach, Radiology **48**:232, 1947.

3. Ewald, C. A., and Boas, J.: Beiträge zur Physiologie und Pathologie der Verdauung, Virchows Arch. f. path. Anat. **104**:271, 1886.

4. Frank, O.: Die Resorption der Fettsäuren der Nahrungsfette mit Umgehung des Brustgangs, Arch. f. Physiol., supp., 1892, p. 497. Matthes, M., and Marguardsen, E.: Ueber die Reaktion des Dunndarminhaltes, Verhandl. d. Cong. f. inn. Med. **16**:358, 1898.

5. Fermi, C.: Ueber die Verdaulichkeit der Speisen im Magen in Beziehung zur Hygiene, Arch. f. Physiol., supp., 1909, p. 1. Pavloff, I. P.: The Work of the Digestive Glands, translated by W. H. Thompson, London, Charles Griffin & Company, Ltd., 1902.

been recognized. Lintwarew [6] noted that fat placed directly in the duodenum caused a decrease in both peristalsis and the secretory activity of the stomach.

While it is probable that neuronal influences are implicated in the inhibition of gastric secretion and motility, Farrell and Ivy [7] demonstrated that humoral agents are also involved, since when fat was fed transplanted and denervated gastric mucosa was observed to act in a way indistinguishable from that portion which had remained in situ. This observation was subsequently confirmed by Lim, Loo and Liu.[8]

An attempt to isolate the humoral material responsible for these effects was successful in 1930. Kosaka and Lim [9] demonstrated that a saline or hydrochloric acid extract of duodenal mucosa which had previously been in contact with fat was able to inhibit gastric activity when administered intravenously. No such effect could be demonstrated when an extract of mucosa which had not been exposed to fat was administered. They proposed that the agent responsible for gastric inhibition be called enterogastrone. This name has been accepted, and in subsequent years enterogastrone has been isolated in increasingly pure form.[10]

Harris, Grossman and Ivy [11] recently demonstrated that relatively pure enterogastrone was not capable of exerting its effect on the denervated dog's stomach. But fat was still able to inhibit hunger contractions in these denervated stomachs.

Little is known of the chemical structure of enterogastrone. It has been determined, however, that none of the digestion products normally resulting from hydrolysis of fat can produce an enterogastrone-like effect and, furthermore, exposure of gastric mucosa to fat will not yield enterogastrone.[12]

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6. Lintwarew, S. J.: Role of Fats in the Transition of the Contents of the Stomach into the Intestines: Experimental Investigation (Russian), Kaiserlich Institut für Experimental Medizin, Thesis, St. Petersburg, 1901; abstracted, Biochem. Centralbl. **1**:96, 1903.

7. Farrell, J., and Ivy, I. C.: Studies on the Motility of the Transplanted Gastric Pouch, Am. J. Physiol. **76**:227, 1926.

8. Lim, R.; Loo, C., and Liu, A.: Observations on the Secretion of the Transplanted Stomach, Chinese J. Physiol. **1**:51, 1927.

9. Kosaka, T., and Lim, R. K. S.: Demonstration of the Humoral Agent in Fat Inhibition of Gastric Secretion, Proc. Soc. Exper. Biol. & Med. **27**:890, 1930.

10. Greengard, H.; Gray, J. S., and Ivy, A. C.: Enterogastrone, Am. J. Physiol. **113**:53, 1935. Gray, J. S.; Bradley, W., and Ivy, A. C.: The Preparation and Biological Assay of Enterogastrone, ibid. **118**:463, 1937.

11. Harris, S. C.; Grossman, M. I., and Ivy, A. C.: The Role of the Vagus Nerves in the Inhibition of Gastric Motility by Fats and by Intestinal and Urinary Extracts, Am. J. Physiol. **148**:338, 1947.

12. Quigley, J. P.; Zettleman, H. J., and Ivy, A. C.: Analysis of the Factors Involved in Gastric Motor Inhibition by Fats, Am. J. Physiol. **108**:643, 1934.

Cannon [13] confirmed the finding of inhibition of gastric motility by fat with the use of roentgenologic studies in which contrast medium was fed along with the fat. In 1932, Nothmann and Wendt [14] demonstrated that the phenomenon of gastric inhibition by fat was no longer present in pancreatectomized dogs. Pratt [15] confirmed this observation. Furthermore, he noted that fat seemed to leave the stomach even more rapidly than simple barium sulfate in the pancreatectomized dogs. Gershon-Cohen and his associates demonstrated by roentgenograms in human beings what they termed the "duodenal mechanism." When fat fed to normal patients reached the duodenum, the pylorus closed and remained closed for long periods. When fat was placed directly in the duodenum, the mechanism operated immediately.[16] The farther down the duodenum fat was placed, the less well the reflex could be demonstrated.[2]

A final observation has been made repeatedly both in pancreatectomized animals [17] and in children with fibrosis of the pancreas.[1] Loss of pancreatic exocrine function results in increased appetite. A concomitant occurrence has been noted: The oral administration of dried pancreas causes an abatement of the increased appetite. These data suggest that the pancreas is involved in the "duodenal mechanism" and that, possibly, enterogastrone is the hormone responsible for the appearance of this mechanism.

METHOD OF STUDY

1. One hundred to two hundred cubic centimeters of a barium sulfate suspension was administered by mouth to selected patients while they were observed under a fluoroscope. The time at which the pylorus opened was noted and was called "zero time." Fifteen, thirty, forty-five and sixty minutes after zero time, roentgenograms of the abdomen were taken with the patient supine.

2. Three to five days later the procedure was repeated, a mixture of 30 per cent fat with barium sulfate being used. The fat used was corn oil.

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13. Cannon, W. B.: The Acid Control of the Pylorus, Am. J. Physiol. **20**:283, 1907.

14. Nothmann, M., and Wendt, H.: Ueber eine regulatorische Funktion des Pancreas für die Magenentleerung nach Fettmahlzeit, Arch. f. exper. Path. u. Pharmakol. **168**:49, 1932.

15. Pratt, J. H.: Pancreatic Disease, J. A. M. A. **120**:175 (Sept. 19) 1942.

16. Gershon-Cohen.[2] Gershon-Cohen, J., and Shay, H.: Experimental Studies on Gastric Physiology in Man: A Study of Pyloric Control; The Role of Milk and Cream in the Normal and in Subjects with Quiescent Duodenal Ulcer, Am. J. Roentgenol. **38**:427, 1937. Shay, H.; Gershon-Cohen, J., and Fels, S.: Role of the Upper Small Intestine in the Control of Gastric Secretion, Ann. Int. Med. **13**:294, 1939.

17. Greenberg, J.: Attempt to Reproduce Cœliac Disease Experimentally in Young Animals by Excluding External Pancreatic Secretions from Intestine, Yale J. Biol. & Med. **6**:121, 1933.

3. After a suitable waiting period (three days), a mixture of barium sulfate and fat was again administered thirty minutes after 3 Gm. of pancreatin had been swallowed. In 2 instances powdered pancreatin U. S. P. was used and in 1 case commercially produced enteric-coated pancreatic granules were used. Observations were again made at prescribed time intervals.

Barium sulfate alone and barium sulfate plus fat were given in succession to 2 normal children who served as controls and to 8 children with fibrosis of the pancreas. The procedure that included giving pancreatin first was carried out on 3 patients with fibrosis of the pancreas.

RESULTS

There was no apparent relationship between the pyloric opening time and the presence or absence of fat in the barium sulfate in either the normal subjects or those with fibrosis of the pancreas.

1. *Normal Controls.*—The procedures in these 2 children yielded similar results. At the initial examination, with no fat in the meal, within fifteen minutes there was considerable gastric emptying. At the end of sixty minutes there was about 50 per cent gastric emptying, with extensive visualization of jejunal and some ileac loops. The mucosal pattern appeared normal throughout with the meal evenly distributed. Reexamination following the meal containing fat showed little barium sulfate passing the pylorus after the initial ejection of a small quantity. The film made fifteen minutes after the beginning of gastric emptying showed scanty amounts of barium sulfate in the upper loops of the small bowel with occasional clumping. In sixty minutes there was only slight additional emptying. The appearance was much like that seen in the so-called deficiency pattern [18] of the small bowel (fig. 1).

2. *Children with Fibrosis of Pancreas.*—In each instance, patients with fibrosis of the pancreas yielded results similar among themselves but quite different from the normal. Examination with the meal containing no fat showed normal emptying at fifteen and sixty minutes, with the meal evenly distributed throughout the small bowel. There was about 50 per cent gastric emptying in forty-five minutes. The second examination, with a meal containing fat, showed prompt gastric emptying, with the upper jejunal loops filled at fifteen minutes and extensive filling of lower loops in forty-five minutes. Roughly 75 per cent gastric emptying was frequently present in forty-five minutes. The distribution of barium sulfate and the appearance of the pattern of the small bowel after the meal with fat were essentially identical with those seen after the meal without fat (fig. 2).

3. *Children with Fibrosis of Pancreas Given Pancreatin.*—The 2 patients who received pancreatin U. S. P. showed the following results:

18. Snell, A. M.: Chronic Idiopathic Steatorrhea: Roentgenologic Observations, Arch. Int. Med. **53**:615 (April) 1934.

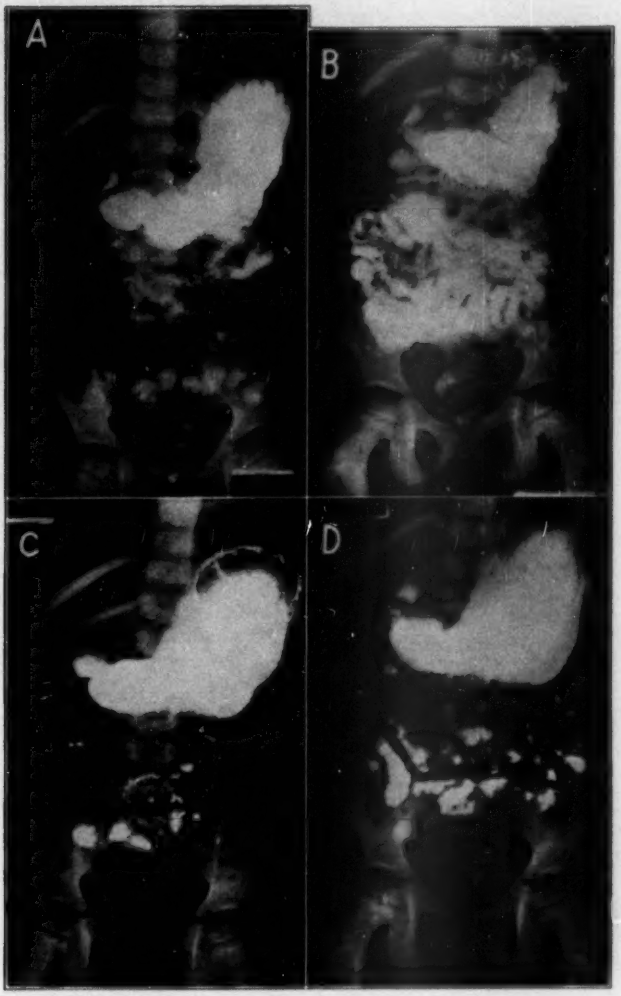

Fig. 1.—Roentgenographic results of studies in normal children. *A* shows amount of gastric emptying in fifteen minutes and *B* in sixty minutes after ingestion of a meal containing no fat. *C* shows the delayed gastric emptying in fifteen minutes and *B* in sixty minutes after ingestion of a meal containing fat.

Gastric emptying following initial opening of the pylorus appeared to be intermittent, and there was clumping of the barium sulfate in the upper loops of the small bowel. The films taken sixty minutes after zero time showed little more than 10 per cent gastric emptying, with a

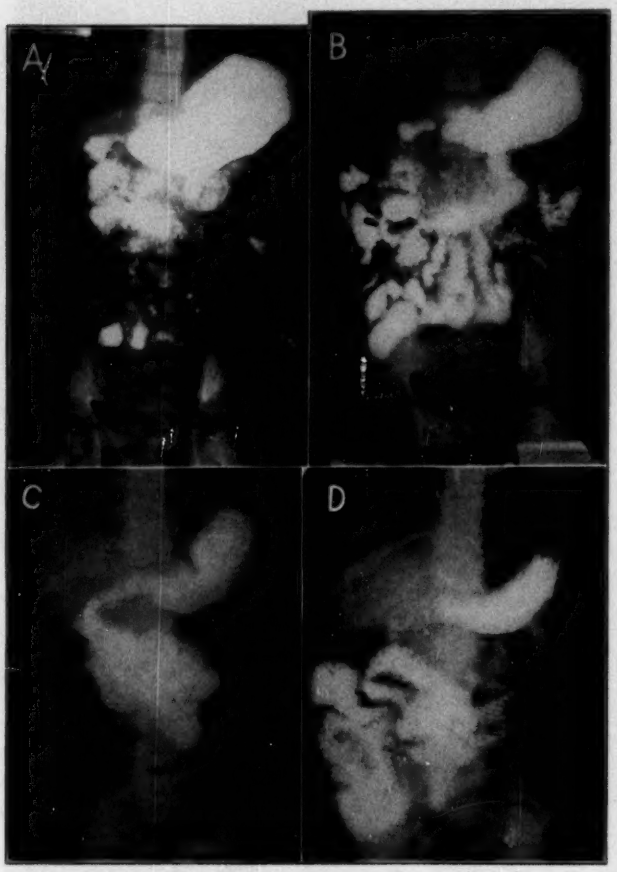

Fig. 2.—Roentgenographic results of studies in children with fibrosis of the pancreas. *A* shows amount of gastric emptying in fifteen minutes and *B* in sixty minutes after ingestion of a meal containing no fat. *C* shows the increased gastric emptying in fifteen minutes and *B* in sixty minutes after ingestion of a meal containing fat.

pronounced tendency toward the variation in caliber of the loops of the bowel and clumping like that observed in the normal patients following administration of a fatty meal (fig. 3).

The patient who was given enteric-coated granules of pancreatin failed to exhibit any findings which differed from those seen during his two previous examinations without it.

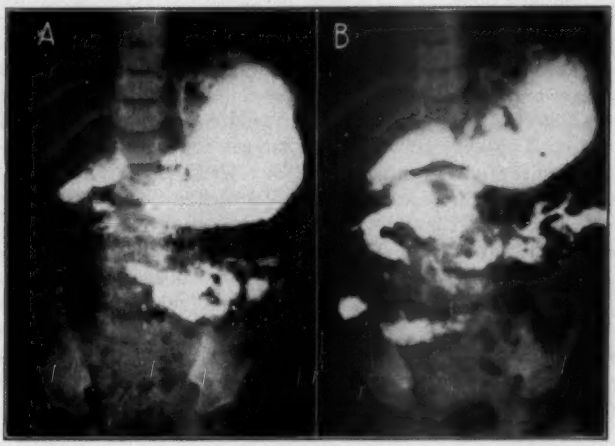

Fig. 3.—Roentgenographic results of studies with administration of pancreatin U. S. P. in addition to a meal containing fat in children with fibrosis of the pancreas. *A* shows delayed gastric emptying after fifteen minutes and *B* after sixty minutes.

COMMENT

It was possible to confirm in patients with fibrosis of the pancreas the observations that Nothmann and Wendt [14] and Pratt [15] had made on pancreatectomized dogs. The normal relationship between gastric motility and emptying time and a fatty meal is not present in patients with fibrosis of the pancreas. If anything, there is decreased gastric emptying time following a fatty meal. The administration of pancreatin U. S. P. thirty minutes before a fatty meal produces an emptying progression in patients with fibrosis of the pancreas quite similar to that found in normal patients following a fatty meal.

The bowel pattern in the children with fibrosis of the pancreas was not unusual either with or without administration of fat. However, in the normal children the pattern when fat was added was typical of the clumping pattern seen in deficiency diseases. This pattern also appeared in the 2 children with fibrosis of the pancreas after the administration of pancreatin U. S. P.

These observations suggest that the humoral agent responsible for the "duodenal mechanism" depends on either a normal pancreas in situ or the products of normal pancreatic digestion. One cannot, on the basis of the present evidence, differentiate between these two possibilities. The pancreatin given by mouth might have been the actual source of this hormone or might have aided in its elaboration when fat was present in the duodenum.

The significance of the deficiency type of bowel pattern observed in normal subjects and in patients with fibrosis of the pancreas is difficult to evaluate. The obvious explanation for it would be that it appears whenever excess fat is present in the bowel. Attractive as that explanation might seem, it does not explain the failure of this pattern to appear in untreated patients with fibrosis of the pancreas or its appearance in them when they were fed pancreatin. A more logical explanation, particularly in view of the work of May and McCreary,[19] who could frequently erase the "clumping pattern" in patients by administration of methacholine (mecholyl®) chloride, is that this intestinal picture is due to the hormone which is responsible for the "duodenal mechanism." The patient with steatorrhea no doubt has residual fat in his intestine at all times, and therefore when barium sulfate is administered one observes the intestinal pattern which normally is present only following the feeding of fat. However, the response per se is due not to the presence of fat but rather to the hormonal effect it has engendered.

CONCLUSIONS

1. In normal subjects orally administered fat results in delayed gastric emptying.

2. In patients with fibrosis of the pancreas the feeding of fat does not have this effect.

3. When pancreatin U. S. P. is fed to patients with fibrosis of the pancreas thirty minutes before a meal with fat delayed gastric emptying results.

4. The interrelation between the normal pancreas, enterogastrone and the "duodenal mechanism" is discussed. It is proposed that these relations may explain the increased appetite observed in patients with fibrosis of the pancreas and its relief by administration of pancreatin.

5. The "deficiency type" roentgenographic pattern was present in the bowel of normal subjects following a meal with fat, but in patients with fibrosis of the pancreas feeding of fat did not produce this effect except after administration of pancreatin. A possible explanation for this observation is advanced.

University of Minnesota (14).

19. May, C. D., and McCreary, J. F.: The Glucose Tolerance Test in Celiac Disease: Significance of Low Blood Sugar Curves, J. Pediat. **17**:143, 1940.

Case Reports

FAMILIAL ERYTHROBLASTIC (COOLEY'S) ANEMIA IN AN AMERICAN INDIAN INFANT

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It is the purpose of this paper to report a case of anemia resembling familial erythroblastic anemia (Cooley's anemia; Mediterranean disease) in an American Indian infant. It is of especial interest because it is believed to be the first case of the condition reported in a person of this race and also because of the extremely early age at which the condition became apparent.

First, however, there may be merit in pointing out the fact that it is increasingly evident that cases of familial erythroblastic anemia are overlooked because the attending physician fails to keep it in mind except when treating descendants of persons of the Mediterranean races.

DISTRIBUTION

It is true that the disease is found largely in those peoples bordering the Mediterranean and their descendents, especially in the Greeks and Sicilians of the northern shores.[1] Those Italians showing the abnormality are stated to be largely of Greek admixture, stemming from the time that the Greeks were undertaking extensive colonization of the whole Mediterranean area.[2]

NOMENCLATURE

In 1925, Cooley and Lee[3] described a brother and sister whose condition was characterized by anemia, splenomegaly and skull changes, associated with a mongoloid appearance. Two years later Cooley and his associates[4] stated that their 7 cases and 5 others reported by Pool and Stillman[5] belonged to a definite clinical syndrome that was distinct from hemolytic icterus or sickle cell anemia. Consequently, Cooley's name was attached to the entity, although he proposed

From the Department of Pediatrics, Jackson Clinic.

1. Diwani, M.: Erythroblastic Anemia with Bone Changes in Egyptian Children: Possible Cooley's Type, Arch. Dis. Childhood **19**:163, 1944.

2. Davison, C., and Wechsler, I. S.: Erythroblastic (Cooley's) Anemia and Neurologic Complications (Status Dysmyelinatus), Am. J. Dis. Child. **58**:362 (Aug.) 1939.

3. Cooley, T. B., and Lee, P.: A Series of Cases of Splenomegaly in Children, with Anemia and Peculiar Bone Changes, Am. J. Dis. Child. **30**:447 (Sept.) 1925.

4. Cooley, T. B.: Von Jaksch's Anemia, Am. J. Dis. Child. **33**:786 (May) 1927. Cooley, T. B.; Witwer, E. R., and Lee, P.: Anemia in Children with Splenomegaly and Peculiar Changes in Bones: Report of Cases, ibid. **34**:347 (Sept.) 1927.

5. Pool, E. H., and Stillman, R. G.: Surgery of the Spleen, New York, D. Appleton & Company, 1923.

the name "erythroblastic anemia."[6] Later, when this term was confused with those for anemias having large numbers of red cells in the circulating blood, such as "erythroblastosis fetalis," Cooley accepted Whipple and Bradford's[7] suggestion of "thalassemia" or "Mediterranean anemia" for the condition.

DIAGNOSIS

The severe anemia which was characteristic of the patients in early case reports made the syndrome readily recognizable, but, recently, investigators[8] have indicated that the disease has a range from the mildest to the severest forms. In fact, the mild forms may include no anemia at all.

The severer forms are characterized by the production of large numbers of abnormal erythrocytes. The cells are usually described as macrocytic except when division has produced microcytes. The cells are hypochromic and appear to be irregularly stained. A striking feature is the large numbers of nucleated erythrocytes. Excessive fragmentation gives rise to numerous irregular forms.

Since 1938, when Bywaters[9] first described the target cell, the presence of such cells in persons with this disease has been well recognized. These cells were described as having "a central, sugar-loaf elevation, so that a cross-section has the appearance of a Mexican hat instead of the normal dumb-bell."[10] On the usual stained smear these cells have a peripheral ring and center that are hemoglobin stained, but the intermediate zone is pale. The finding of these cells, however, is not limited to this syndrome.

The presence of decreased cell fragility was confirmed by Dameshek.[11]

Besides the striking blood picture, there may be other diagnostic criteria, such as the mongoloid facies. A protruding abdomen may result from the splenic enlargement, and pallor and anorexia are not uncommon. Bone changes are serious and appear on roentgenograms as bony striae.

PREVALENCE

Cooley's original cases consisted of 5 occurring in children of the Mediterranean races but also included 1 of an English girl and 1 of a mulatto boy that

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6. Cooley, T. B.: Likenesses and Contrasts in the Hemolytic Anemias of Childhood, Am. J. Dis. Child. **36**:1257 (Dec.) 1928.

7. Whipple, G. N., and Bradford, W. L.: Mediterranean Disease–Thalassemia: Associated Pigment Abnormalities Simulating Hemochromatosis, J. Pediat. **9**:279, 1936.

8. (*a*) Smith, C. H.: Mediterranean Anemia in Youth of Nineteen Years Observed Since Early Childhood: Familial Aspects and Hematologic Features of "Carrier" or Asymptomatic Case, J. Pediat. **20**:370, 1942. (*b*) Wintrobe, M. M.; Matthews, E.; Pollack, R., and Dobyns, B. M.: Familial Hemopoietic Disorder in Italian Adolescents and Adults Resembling Mediterranean Disease (Thalassemia), J. A. M. A. **114**:1530 (April 20) 1940.

9 Bywaters, E. C. L.: Cooley Syndrome in an English Child, Arch. Dis. Childhood **13**:173, 1938.

10. Haden, R. L., and Evans, F. D.: Sickle Cell Anemia in the White Race: Improvement in Two Cases Following Splenectomy, Arch. Int. Med. **60**:133 (July) 1937.

11. Dameshek, W.: "Target Cell" Anemia: Anerythroblastic Type of Cooley's Erythroblastic Anemia, Am. J. M. Sc. **200**:445, 1940.

were later withdrawn from consideration. However, it has become increasingly evident that the distribution of this disease cannot be limited to the descendants of persons of the Mediterranean races, and Downey [12] stated that many cases must have been overlooked because they did not fit into the correct racial pigeonhole.

Gradually, there is accumulating evidence that persons of other races may be affected. Bones removed from mounds of the pre-Columbian Peruvians [13] have an identical roentgenologic appearance as those of their modern counterparts with familial erythroblastic anemia.

Four cases have been reported in those of Turkish descent,[14] and a number have been described in East Indians. Mukherji [15] observed the condition in a 30 month old Hindu baby. Patel and Bhende [16] described it in a Brahmin boy who had additional complications of cirrhosis of the liver and kyphosis. Coelks [17] observed it in 2 girls of the same race, and Napier [18] and his associates reported it in another Brahmin boy. Malhotra and Chhuttani [19] reported a case from New Delhi.

In 1940, Foster [20] reported the first case among the Chinese, and in the same year Wang and Khoo [21] described 3 cases of erythroblastosis in Chinese children, 1 of whom appeared to have familial erythroblastic anemia. Sendrail and his associates [22] reported a case of a Spanish child.

The Negro race has not been by-passed, as Dameshek [23] observed a Negro child with typical findings. He said that he has often seen target cells in Negroes without sickling and stated that the entire subject needs amplification.[24]

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12. Downey, H.: Handbook of Hematology, New York, Paul B. Hoeber, Inc., 1938, vol. 3.

13. Atkinson, D. W.: Erythroblastic Anemia: Report of Two Cases in Adult Siblings, with Review of Theories as to Its Transmission, Am. J. M. Sc. **193**:376, 1939.

14. Saracoglu, K.: Cooley's Anemia in Turkey, Wien. med. Wchnschr. **93**:217, 1943.

15. Mukherji, M.: Cooley's Anæmia (Erythroblastic or Mediterranean Anæmia), Indian J. Pediat. **5**:1, 1938.

16. Patel, N. D., and Bhende, Y. M.: Erythroblastic Anæmia with Kyphosis and Cirrhosis of Liver, Indian J. Pediat. **6**:217, 1939.

17. Coelks, G.: Erythroblastic Anemia—Cooley's Anaemia, M. Bull., Bombay **7**:291, 1939.

18. Napier, L. E.; Shorten, J. A., and Das Gupta, C. R.: Cooley's Erythroblastic Anæmia, Indian M. Gaz. **74**:660, 1939.

19. Malhotra, R. P., and Chhuttani, P. N.: Case of Cooley's Anæmia, Indian M. Gaz. **79**:198, 1944.

20. Foster, L. P.: Cooley's Syndrome (Erythroblastic Anemia) in a Chinese Child, Am. J. Dis. Child. **59**:828 (April) 1940.

21. Wang, C. Y., and Khoo, F. Y.: Hemolytic Anemia with Erythroblastaemia: Report of Three Cases Seen in Chinese Infants, Chinese M. J. **58**:177, 1940.

22. Sendrail, M.; Lyon, A., and Lasserre, J.: Infantilisme splénique de type Cooley, Bull. et mém. Soc. méd. d. hôp. de Paris **52**:902, 1936.

23. Dameshek, W.: Familial Mediterranean Target Oval Cell Syndromes, Am. J. M. Sc. **205**:643, 1943.

24. Dameshek, W.: Medical Progress: Hematology, New England J. Med. **234**:829, 1946.

Bywaters[9] found the condition in an English child, giving added emphasis by saying that she had a blue-eyed English policeman as a father and an English mother.

GENETICS

Wolman and Dickstein[25] gave a noteworthy summary of the genetic behavior of the disease and stated that an incomplete recessive gene is at fault. Cooley[26] presented an opposite view; he expressed the opinion that it is inherited by a simple dominant mechanism and that the disease is not race limited. He observed: "... When a disease-producing mutation takes place, it is evident that it will recur first in the neighborhood of its origin.... It will be limited to a community, a province or a race in proportion to the clannishness and the isolation of the people involved.... a proved case of sickle cell anemia in a Peloponnesian or of Mediterranean amenia in a Chinese child in Hawaii must [not] be ascribed to an unlikely racial cross.... It is only common sense to explain such occurrence as new appearance of the mutations, which may, of course, set up new foci of the dieases."

Although the genetic pattern is somewhat clouded at present, there seems to be little doubt that the condition has a hereditary origin. Evidently, the patients with the milder forms may reach adulthood and procreate, while those with the severer forms usually fail to reach maturity, or, if they do, they fail to reproduce.[27] On the other hand, the literature is increasingly filled with reports of long survival after diagnosis of the disease. To name only 2 examples, Wintrobe and his co-workers[8b] followed one Sicilian with well established findings for ten years, and Atkinson[18] had 2 adult siblings of Greek extraction under his care for twelve years.

Now that it is evident that there are many persons with the mild forms acting as a reservoir, one may speculate that the condition will become more widespread by the interplay of hereditary factors.

REPORT OF A CASE

I wish to present a case history of a male American Indian infant first seen at the age of 2 months because of an umbilical hernia. The rupture had been noted one month before and was rapidly becoming more prominent. The ancestry on the father's side was pure, but the mother was reported to have had a French great-grandmother. There had been no abnormalities of birth, although the infant had been premature with a weight at birth of 4 pounds 7 ounces (2,012.8 Gm.). The present weight was 8 pounds 1½ ounces (3,671.3 Gm.). Results of physical examination were essentially normal except for the hernia, which was reduced and held in place by a broad adhesive dressing. Blood counts were not made.

The infant was returned to the hospital three weeks later with multiple complaints. For the previous week he had been crying much of the time. Abdominal distention was present; he had much flatus and loose stools for two days. There was no fever or vomiting.

The most impressive feature was a jaundice, striking even in his copper skin. The liver and spleen were not palpable and the hernia was showing satisfactory reduction. There was no sign of an infectious process.

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25. Wolman, I. J., and Dickstein, B.: Changing Concepts in Mediterranean Anemia, Am. J. M. Sc. **212**:723, 1946.

26. Cooley, T. B.: Hereditary Factors in the Blood Dycrasias: President's Address, Am. J. Dis. Child. **62**:1 (July) 1941.

27. McIntosh, R., and Wood, C. L.: An Inquiry into the Genetic Factor in Cooley's Anemia, Am. J. Dis. Child. **64**:192 (July) 1942.

The icteric index was 99.8 units. The urinary test for bile gave a faintly positive reaction, and bile was present in the stool.

The blood presented the most interesting picture. The red blood cell count was 2,670,000, the white blood cell count, 21,900 and the hemoglobin concentration, 8.5 Gm. (51 per cent). Anisocytosis and poikilocytosis were prominent, with a tendency toward macrocytosis. There was an occasional Howell body. Reticulocytes made up 10 to 15 per cent of the total. Many cells were basochromic and the so-called target cells were common.

In making a count of 100 white cells, 26 nucleated red cells were seen, many of which were macroblasts. The differential count was as follows: neutrophils, 17 (segmented, 11; band forms, 6); lymphocytes, 72; lymphoblasts, 2; eosinophils, 4, and unidentified forms, 5, per hundred cells.

No sickling of the red cells was noted even under decreased oxygen tension. Tests revealed decreased cell fragility; initial hemolysis began at 0.34 per cent and was complete at 0.28 per cent (the control showed initial hemolysis at 0.44 per cent and hemolysis was complete at 0.38 per cent). A van den Bergh test was not done. Unfortunately, no roentgenograms of bone were made.

An initial transfusion of 100 cc. of whole blood was given, followed two days later by one of 75 cc. The jaundice faded gradually during the next one and one-half weeks that he remained under observation, but the blood picture did not show much improvement. The red blood cell count did not rise above 2,900,000, and the hemoglobin concentration was essentially the same. The white blood cell count fell to 8,950, but the stained smear showed little tendency to return to normal.

The mother was confronted with a family problem which caused her to return to the reservation with the infant, and he passed from my observation.

From this point I have only the statement of the local physician who did not see the patient until approximately four months later, at which time the infant was moribund. A "cold" had been contracted a few days previously with a complicating bronchopneumonia. No blood counts were made before his death, as the physician was not told of the previous history.

At my request, the physician called the mother who stated that the infant had appeared "all right" to her and was gaining weight until the infection of the upper respiratory tract occurred.

COMMENT

This case presented a problem in differential diagnosis. Due to the severe jaundice and gastrointestinal complaints, I first considered the diagnosis of an obstructive jaundice. However, the stools were not acholic, and after the first transfusion the gastrointestinal complaints disappeared. The anemia was revealed on blood count, which directed attention to other causes.

Erythroblastosis fetalis also had to be considered. However, the jaundice did not appear until late in the second month, and the mother, father and infant were all Rh positive.

Hemolytic icterus was a possibility. However, the infant's blood had a diminished resistance to hemolysis by hypotonic solution and did not have the microcytosis or spherocytes usually observed.

Sickle cell anemia was ruled out by failure to demonstrate sickling. The parents denied any Negro mixture.

Pernicious anemia almost never occurs in infants, and this patient did not have the high color index or leukopenia usually seen in persons with pernicious anemia.

The father, mother and infant had negative reactions to the Kahn test for syphilis.

Chronic secondary anemia did not seem a possibility, since the condition appeared as an acute process which reached its peak after the first visit to the hospital and was not accompanied with any infectious process.

Criteria for diagnosis of megaloblastic anemia of infancy, as reported by Zuelzer and Ogden,[28] appeared not to be satisfied in this instance.

With familial erythroblastic anemia left as the chief possibility, the condition of the patient did not fit all the usual diagnostic criteria. I thought, however, that absence of splenomegaly and the severe jaundice could be explained on the basis of his immaturity. By racial characteristic this infant already had the mongoloid-like facies that usually does not appear in the affected persons until after the first year. It is unfortunate that roentgenograms of bone were not made, but one author stated that the bone changes do not come until after the blood changes.[29] They have been observed in infants as young as 4½ months, though usually not appearing until the sixth to ninth months. With hereditary factors in mind, a count made on the mother's blood showed no abnormality. The father was not available for such a study.

SUMMARY

A case of familial erythroblastic anemia (Mediterranean disease; Cooley's anemia) in a male American Indian infant 2¼ months of age is presented. It is of especial interest because it is believed to be the first case of this condition reported in a person of this race and also because of the early age at which the condition became apparent.

16 South Henry Street (3).

28. Zuelzer, W. W., and Ogden, F. N.: Megaloblastic Anemia in Infancy: Common Syndrome Responding Specifically to Folic Acid Therapy, Am. J. Dis. Child. **71**:211 (March) 1946.

29. Caffey, J.: Skeletal Changes in Chronic Hemolytic Anemia, Am. J. Roentgenol. **37**:293, 1937.

INFANTILE CORTICAL HYPEROSTOSIS

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SEVERAL cases of the syndrome of infantile cortical hyperostosis have been reported since Caffey and Silverman [1] first described this heretofore unknown disease of infants. Smyth, Potter and Silverman [2] were among the early workers to add to the rapidly growing number of cases. These were followed with reports by Whipple,[3] Dickson and his associates,[4] Shuman [5] and Gipson and Clark [6] and from the Children's Hospital, Washington, D. C.[7] The purpose of this report is to present 2 additional cases of this syndrome and to discuss some variable aspects of the disease.

REPORT OF CASES

CASE 1.—M. A. F., a 5 month old Italian infant, was admitted to the babies' wards of the New York Post-Graduate Hospital on Nov. 11, 1947 because of a facial swelling since 2 weeks of age.

Family History.—The parents were living and in good health. There were no known familial diseases.

Birth History.—This was the first pregnancy. The infant was full term and was delivered without difficulty. The weight at birth was 5 pounds 8 ounces (2,494.8 Gm.) and there was no asphyxia or convulsions or other neonatal disturbances. The mother had no illness during the pregnancy.

From the Department of Pediatrics, New York University-Bellevue Medical Center, University Hospital (formerly New York Post-Graduate Hospital).

1. Caffey, J., and Silverman, W. A.: Infantile Cortical Hyperostosis: Preliminary Report on a New Syndrome, Am. J. Roentgenol. **54**:1, 1945. Caffey, J.: Infantile Cortical Hyperostosis, J. Pediat. **29**:541, 1945.

2. Smyth, F. S.; Potter, A., and Silverman, W.: Periosteal Reaction, Fever and Irritability in Young Infants: A New Syndrome? Am. J. Dis. Child. **71**:333, (April) 1946.

3. Whipple, R. K.: Infantile Cortical Hyperostosis: Report of a Case, New England J. Med. **236**:239, 1947.

4. Dickson, D. D.; Luckey, C. A., and Logan, N. H.: Infantile Cortical Hyperostosis, J. Bone & Joint Surg. **29**:244, 1947.

5. Shuman, H. H.: Infantile Cortical Hyperostosis: Case Report, J. Pediat. **32**:195, 1948.

6. Gipson, A. C., and Clark, B. P.: Infantile Cortical Hyperostosis, Pediatrics **1**:221, 1948.

7. Conference on Infantile Cortical Hyperostoses (Caffey-Smyth Syndrome), Conference of Children's Hospital, Washington, D. C., J. Pediat. **32**:441, 1948.

Past History.—The infant was given an adequate evaporated milk formula with a vitamin supplement and was apparently well until the onset of the present illness.

Present Illness.—At the age of 2 weeks the infant had a pustular eruption of the neck. This was treated with topical application of medicaments and the lesions disappeared in a few days. At the same time, the parents noted an asymmetry of the face caused by a swelling of the right side of the jaw. The swelling slowly increased in size but never showed any discoloration. It "felt hard," and the infant cried out with pain whenever it was touched. No treatment was instituted and the patient was observed for several weeks. The swelling fluctuated in size, becoming larger and smaller, though untreated. On October 3, when the infant was 4 months of age she was admitted to another institution for diagnosis and treatment. The lesion was described there as a "large, stony hard, subcutaneous, well defined, immobile mass, measuring 4 cm. in diameter at the angle of the right mandible." There was no limitation of movement of the jaw. The highest temperature recorded was 100.4 F. Laboratory tests revealed a normal blood count, no abnormality on urinalysis and a negative blood Wassermann reaction. A roentgenogram of the right side of the face revealed a soft tissue mass over the angle of the right mandible. The appearance of the chest on a roentgenogram was reported to be normal. A biopsy specimen of the mass revealed chronically inflamed tissue. The course in the hospital was reported as uneventful; the mass diminished in size and the infant was discharged on October 18, with the diagnosis of chronic inflammation (right mandibular area). The facial swelling recurred, and the patient was treated at home for several days with sulfadiazine and penicillin. The latter was administered both orally and intramuscularly, and there was an immediate reduction in the facial edema, but swelling recurred when the treatment was discontinued. It was then felt that there was a bony involvement of the right mandible and hospitalization was advised.

Physical Examination.—The infant appeared pale but well developed and well nourished. The right side of the face revealed a large mass which produced a striking asymmetry (fig. 1). The skin was not discolored and there was no increased warmth. There was a brawny edema, indurated and immobile, which appeared to be continuous with the mandible. Slight limitation of motion of the jaw was present. The infant was irritable and cried on attempts at palpation of the mass. The remainder of the examination revealed nothing abnormal.

Laboratory studies showed 4,050,000 red blood cells, a hemoglobin concentration of 9.5 Gm. and a white blood cell count of 18,000, with 67 polymorphonuclear cells, 28 lymphocytes and 5 monocytes, per hundred cells. Anisocytosis, achromia and poikilocytosis were present. Urinalysis gave normal results. Roentgenograms made on November 12 were reported on as follows (fig. 2): "Examination showed a disarrangement of the cancellous structure, with evident enlargement in the transverse diameter of the mandible on the right side, this involving practically the whole of the body up to and beyond the symphysis. In addition to the general enlargement of the mandible on this side, there are periosteal lift and productive changes (apparently formation of involucrum) suggesting an osteomyelitis as the most likely factor."

Course in the Hospital.—The infant was offered a regular diet for a child her age with supplemental vitamins. Because of the anemia, two transfusions of 120 cc. of whole blood were given. Extreme irritability was controlled by the use of sedatives. Intensive treatment with penicillin was started, with the administration

of 50,000 units every three hours. To this was added sulfadiazine, 1½ grain (0.09 Gm.) every three hours. After three days of treatment, the penicillin was increased to a total of 600,000 units daily. After ten days, the use of sulfadiazine was discontinued. Penicillin was given in this dosage for thirty-five days, after which the dose was decreased to 25,000 units every three hours, with the addition of carinamide, 0.25 Gm., and this was administered for the next ten days. A total of 22,200,000 units of penicillin was given during a thirty-eight day period. Two days after treatment with penicillin was begun, the swelling, edema and tenderness of the right cheek, jaw and submaxillary area were noted to be considerably decreased. This decrease was progressive and at the end of one month examination revealed nothing but a bony enlargement of the mandible. Repeated roentgenologic examination at monthly intervals revealed the condition as first reported. The last report on December 12 was as follows: "Reexamination of the mandible shows the evident enlargement in the transverse diameter on the right side with periosteal elevation practically as last reported. There is no definite evidence of

Fig. 1 (case 1).—Photograph showing characteristic facial asymmetry.

destruction of the cancellous structure." The patient's illness ran an afebrile course in the hospital and she gained 1 pound (453.6 Gm.) during her fifty-eight days of hospitalization. The blood cell count on her discharge was within normal limits. The diagnosis on discharge was probable osteomyelitis of the right mandible.

The patient remained asymptomatic for two weeks after her discharge, when there was a recurrence of the swelling and edema of the right cheek. At this time the diagnosis of infantile cortical hyperostosis was entertained. The roentgenograms of the jaw were reviewed and the diagnosis was confirmed. The entire skeletal structure was then examined roentgenographically, and all other bones were reported as normal. Since the diagnosis was established, the patient has been treated symptomatically. There have been several recurrences, but each time the swelling is definitely smaller and causes less discomfort. The patient's progress in growth and development is normal.

CASE 2.[8]—J. T., a 2 month old white male infant, was admitted to the hospital on Jan. 21, 1948 because of edema of the lower extremities and extreme irritability which were first noted by the parents when he was 5 weeks of age.

Family History.—The parents were living and enjoying excellent health. There were no known familial diseases. There was one sibling 2½ years of age who was born five weeks prematurely. This child had had no diseases of the newborn; she gained satisfactorily, and her growth and development were normal.

Birth History.—This was the second pregnancy with the spontaneous delivery of a premature infant weighing 3 pounds 9 ounces (1,615.9 Gm.). Cyanosis was noted at birth, and the infant required oxygen for twenty-four hours. The exact nature of this disturbance is not known. Because of prematurity the patient remained in the nursery for five weeks and was given an adequate powdered milk formula with vitamin supplement. There was a progressive gain in weight and the entire hospitalization was described as uneventful.

Present Illness.—On the arrival at home the mother first noted that the infant's feet were swollen. The swelling became progressively worse and spread upward to involve the legs. When the infant was 2 months of age, the edema was said to involve the entire lower extremities and the scrotum. At this time, some swelling of the dorsa of the hands and puffiness of the eyes were also present. The infant was extremely irritable and cried a great deal. The stools were normal in character and number and the formula was taken well.

Physical Examination.—The patient was well developed and well nourished. The head measured 14⅛ inches (35.9 cm.); the chest, 13¼ inches (33.7 cm.), and the length, 19¼ inches (48.9 cm.). The skin appeared pale and there was an obvious pitting edema of the pretibial areas of both legs and on the dorsa of the feet. The upper lids were decidedly swollen. The scrotum was swollen, but there was no other abnormality of this area. A small umbilical hernia was evident. Pronounced irritability and a fine tremor of the lower jaw and the hands were noted.

Laboratory Data.—A blood count revealed 3,000,000 red cells per cubic millimeter, a hemoglobin concentration of 7.7 Gm. per hundred cubic centimeters, and a white cell count of 5,800 per cubic millimeter, with 29 polymorphonuclear forms, 6 eosinophils, 2 basophils, 5 lymphocytes, 6 monocytes and 1 normoblast per hundred cells. Anisocytosis was moderate, with occasional microcytosis and macrocytosis. Erythrocytes showed polychromasia. Blood chemical studies revealed nonprotein nitrogen to be 26 mg., urea nitrogen 16 mg., total cholesterol 75 mg., cholesterol esters 35 mg., inorganic phosphate 5.8 mg., total calcium 10.9 mg., alkaline phosphatase 10 mg. (Bodansky units), total protein 4.8 Gm., albumin 2.9 Gm. and globulin, 1.9 Gm., per hundred cubic centimeters. The albumin to globulin ratio was 1.5:1. Chlorides present as sodium chloride were 525 mg. per hundred cubic centimeters. The blood Wassermann reaction was negative. The urinalysis showed a trace of protein.. Roentgenologic study of the lower extremities on January 23 was reported on as follows: "There is considerable periosteal proliferation of the shafts of the long bones, but no other definite findings and no particular anemia that might suggest a special bony disease entity are present." The condition was concluded to be periosteal proliferation. A vitamin A absorption test performed at the age of 5 months revealed a fasting level of 10 blue units and a rise to 40 blue units, per hundred cubic centimeters, three

8. This patient was from the pediatric service of Dr. Adolph G. DeSanctis.

hours after ingestion of a test dose of 0.1 cc. of percomorph liver oil (oleum percomorphum) per pound of body weight.

Course in the Hospital.—A diagnosis of nutritional edema with a secondary anemia was entertained. The patient was given an adequate formula with vitamin supplement. A transfusion of 100 cc. of whole blood was given to correct the anemia. Without any further therapy the edema of the eyes and legs decreased after eight days of hospitalization. During the entire course in the hospital the patient remained afebrile. He was discharged on the tenth day only slightly

Fig. 2 (case 1).—Roentgenogram of jaw made on patient's admission to the hospital showing involvement of the right mandible.

improved. On follow-up observation in the outpatient department roentgenologic examination of the entire skeletal structure revealed involvement of only the long bones of the lower extremities. A roentgenogram of the chest showed moderate thymic enlargement. Since the swelling of the lower extremities had recurred from time to time, the roentgenograms were reviewed and the diagnosis of infantile cortical hyperostosis was made. The patient was last seen at 5 months of age. The weight was 14 pounds 5 ounces (6,492 Gm.); the blood count showed 4,510,000 red cells per cubic millimeter, a hemoglobin concentration of 10.3 Gm. per hundred cubic centimeters and 9,050 white cells, with 17

polymorphonuclear cells, 5 eosinophils, 72 lymphocytes and 6 monocytes, per hundred cells. There was still a moderate brawny edema of the tibial areas. However, the infant was thriving and appeared to be normal in growth and development.

COMMENT

In the first patient we noted a definite improvement with a decrease in the soft tissue swelling and diminished pain following the use of large doses of penicillin. This is the first case reported in which some amelioration of symptoms has followed treatment with penicillin. This was perhaps due to the massive doses given over a period of thirty-eight days, since we felt at first that the diagnosis was osteomyelitis of the mandible. The facial edema in this patient was absent for approximately two months. This remission occurred during treatment with penicillin and continued for several weeks following cessation of therapy. Even prior to hospitalization it was noted that the edema of the face decreased with intensive penicillin therapy. A history of onset at 2 weeks of age with a concomitant pustular eruption of the neck has not been reported by other observers. This may be a clue to the possible causation of this condition, with the skin being the portal of entry of some infectious agent, or the occurrence of the rash and the edema of the face may be coincidental. Like most others reported on, this patient had an elevation of temperature at one time, leukocytosis, anemia, facial swelling, irritability and positive roentgenologic findings of cortical hyperostosis. The report on biopsy of chronic inflammation seems to substantiate the impression that this condition is caused by an infectious agent.

The second case reported is unusual because of the unquestionable pitting edema of the patient's lower extremities when he was first seen. This pitting receded, but on later examination it appeared as a hard brawny edema. This is the first case reported in which there was noted a moderate eosinophilia that to date has remained constant. Because of a similarity in the bony changes to those in hypervitaminosis A as reported by Toomey and Morissette,[9] a vitamin A absorption test was performed but results were observed to be within normal limits. This possible etiologic factor has not heretofore been suggested. It is hoped that with the increasing number of cases being reported, interest will grow and stimulate workers to probe further into the nature of this condition.

SUMMARY

Two cases of infantile cortical hyperostosis are reported. The facial edema of 1 patient subsided temporarily during an intensive course of penicillin therapy. Possible etiologic factors are suggested.

123 East Eighty-Third Street (28) (Dr. Larkin).

Permanente Foundation Hospital (Dr. Rousseau).

9. Toomey, J. A., and Morissette, R. A.: Hypervitaminosis A: Case Report, Am. J. Dis. Child. **73**:473 (April) 1947.

CONGENITAL DIVERTICULOSIS OF LEFT VENTRICLE

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Congenital diverticulosis of the left ventricle is an extremely rare maldevelopment. The following case of sudden or unexpected death is reported because of this finding.

REPORT OF A CASE

Baby boy S., a full term white male infant, was delivered by low forceps at the Jewish Hospital of Brooklyn at 6 p.m. on Jan. 5, 1947. The mother was a 30 year old primipara whose pregnancy was uneventful. The first stage of labor lasted twelve and one-half hours and the second stage two and one-half hours.

The patient had a slightly delayed, weak cry, grunting respirations and moderate cyanosis. The weight at birth was 7 pounds 5 ounces (3,316.9 Gm.). There was moderate molding of the skull but no caput succedaneum or external signs of injury to the scalp or skull. Oxygen and vitamin K subcutaneously were administered. Physical examination two hours after birth revealed a good cry, cyanosis of the extremities and mucous membranes, normal heart sounds and no murmurs. The lungs were clear to percussion and auscultation except for slight diminution of breath sounds over the upper lobe of the left lung. Use of oxygen was continued. Examination six hours after birth revealed no cyanosis; the cry was vigorous; respirations were regular; the heart sounds were of good quality with no murmurs heard, and the lungs were normal to percussion and auscultation. Slight tremors of the extremities were noted on exposure. During the second half of the first day of life the patient did not suck vigorously but did manage to take 1 ounce (30 cc.) of formula every four hours. He was able to maintain good color without oxygen; respirations and cry were normal, and nothing abnormal was noted on physical examination except for coarse tremors when the infant was stimulated.

At 7:30 a.m. (approximately thirty-eight hours after birth) on January 7, after having appeared comfortable, feeding relatively well and maintaining good color without oxygen all night, the patient, who was not being fed at the time, suddenly became cyanotic and died almost immediately.

The clinical impression was cerebral birth injury or cerebral anoxia.

At autopsy, the body was that of a well developed and well nourished white infant, 50 cm. in length and weighing approximately 3,300 Gm. The peripheral portions of the body were cyanotic. The veins of the neck were distended. There

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was partial collapse of the lungs. The pericardial cavity contained 60 cc. of blood. The heart weighed 20.5 Gm.

There were petechiae beneath the epicardium near the base. The atriums were dilated. In the ventricular pocket behind the aortic cusp of the mitral valve was an opening, 0.4 by 0.5 cm., which was lined by endocardium continuous with that of the left ventricle. This opening led into a diverticulum which

Photomicrograph of diverticulum showing thrombotic material attached to endocardial surface. Note thinness of the sac. Stained with hematoxylin and eosin.

bifurcated, forming two bulbous sacs. These projected posteriorly and laterally and lay against the medial wall of the left atrium and the left side of the pulmonary artery. The bulbous terminations were 0.9 cm. in diameter and the walls were composed of all the heart layers, histologically. There was a perforation of one sac. The apex of the other sac was paper thin. Both contained

thrombotic material. The ductus arteriosus was patent. The remainder of the heart was not remarkable. There were no other significant autopsy observations.

The anatomic diagnoses were diverticulum of the heart with rupture, hematopericardium, patent ductus arteriosus, atelectasis and congestion of viscera.

COMMENT

True congenital cardiac aneurysms or diverticulums are extremely rare. A review of the recent literature reveals few cases. Arnold [1] described true congenital diverticulums as finger-like and associated with defects in the development of the pericardium, sternum and abdominal wall. He reported a case with these observations in a 1½ month old infant and listed cases with similar findings as reported by Mahrburg, von Dietlen, Giebert and Bryan. Norman and Taylor [2] described a congenital diverticulum in a patient with epiloia. Bayer [3] reported 3 cases, 2 of which were of elderly adults and 1 of an infant. Von Sydow [4] described a case of an 8 year old girl in whom rupture occurred. Drennan and van der Vijver [5] had a similar case of a 4 year old child who died suddenly while at play.

The case presented is the first seen in this hospital. The defect is also unique in that no other intrinsic cardiac anomalies were present except for the patent ductus. According to the literature, this is by far the youngest patient having the lesion with rupture thereof.

The mechanism of formation of congenital diverticulum has been extensively discussed, but conclusions have been only conjectural. It has been postulated that intracardiac pressure directed at a weak area may be partly responsible. During the formation of the leaflets of the cardiac valves, excrescences develop from the respective aperture walls which represent the endocardial cushions. These cushions are invaded initially by muscle. Soon, the muscle degenerates and is replaced by fibrous tissue in the valve leaflets and chordae tendineae, all of which are covered by endothelial cells. Fibrous tissue develops around the apertures and serves as a skeleton for the cardiac muscle. These rings fuse centrally and form a triangular structure known as the trigonum fibrosum. Portions of the interventricular and interatrial septums are involved in this structure. The right anterior portion of the mitral ring fuses with the ring of the aortic valve at this point. The fibrous rings on the left side are strongest.

In this case the opening from the heart into the diverticluum occurred just inferior to and to the left of this point of central fusion. Therefore, the defect was in the musculature per se, since the mitral valve ring was intact. The

1. Arnold, J.: Ueber angeborne Divertikel des Herzens, Virchows Arch. f. path. Anat. **137**:318-329, 1894.

2. Norman, R. M., and Taylor, A. L.: Congenital Diverticulum of the Left Ventricle of Heart in a Case of Epiloia, J. Path. & Bact. **50**:61-68, 1940.

3. Bayer, J.: Diverticula of the Heart, Virchows Arch. f. path. Anat. **306**:43-52, 1940.

4. von Sydow: Ruptur des Herzens bei einem Kinde, J. f. Kinderk. **47**:437, 1866.

5. Drennan, M. R., and van der Vijver, G. T.: Diverticulum of the Human Heart, J. M. A. South Africa **2**:58-60, 1928.

etiologic basis for this true diverticulum can be postulated as a defect in muscular attachment to the mitral ring at that point. Subsequently, pressure, which is greatest on this side, caused the outpouching of all the layers of the heart. Since blood stagnated here, thrombosis was encouraged. Constant pounding on this thinned-out sac resulted finally in perforation, with pericardial tamponade and sudden death.

SUMMARY

A case of ruptured diverticulum of the left ventricle is presented and discussed.

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ESCHERICHIA COLI MENINGITIS TREATED SUCCESSFULLY WITH STREPTOMYCIN

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ESCHERICHIA coli meningitis is rather unusual. It is observed particularly in newborn children, who, according to Scherer [1] are infected through a bacillemia. Cases in infants, 2 months old, were observed by Reinhardt [1a] and Navarro.[1b] Navarro stated that until 1929 he had found in the literature only 18 cases of E. coli meningitis in children. It is also reported as occurring during infancy subsequent to gastric disturbances.[2] The spinal fluid is not clear but usually purulent.

The mortality rate of reported cases of this disease is high. Bardisian,[3] in seventeen years of his pediatric career, observed only 4 cases and death occurred in all within a few days. It is true that for many years the treatment was more empiric and was unsuccessful, until the discovery of streptomycin and the observation that it exhibited a powerful bacteriostatic activity against many of the gram-negative pathogens.[4] After a review of the experiments which showed that E. coli is also susceptible to the action of streptomycin, we thought, as soon as we made the diagnosis of meningitis due to E. coli in the following case, that this antibiotic substance should be tried.

REPORT OF A CASE

A boy, 2½ years old, entered our clinic March 27, 1948, with symptoms of meningitis. He was the only child of healthy parents, and his growth had been normal. He weighed 12.2 Kg. According to the parents, he had had no previous illness. For the past four days there were elevation in temperature, headache and vomiting. Penicillin was administered without improvement.

On examination, the tongue was pale and glazed; the abdominal muscles were slightly contracted. The liver and spleen were within their normal limits. Rales were heard over the lower posterior portions of the lungs. The temperature was 101.5 F. Tachycardia was present. No disturbances of the sensorium

1. Scherer, cited by Comby, J.: Traité des maladies de l'enfance, ed. 5, Paris, J. Rueff, 1907.

1a. Reinhardt, I.: Monatsschr. f. kinderh. **38**:341, 1927.

1b. Navarro, I. C.: Arch. españ. de pediat. **13**:513 (Sept.) 1929.

2. Nobécourt, P., and Du Pasquier: Bull. Soc. de pédiat. de Paris **4**:371, 1902. Ducasse, P. G., and Dupérié, R.: Compt. rend. Soc. de biol. **96**:407 (Feb. 18) 1927.

3. Bardisian, A.: Pediatria **38**:777 (July 15) 1930.

4. Janney, F. R.; Conway, J. P., and Beck, K. H.: J. Pediat. **30**:459 (April) 1947.

were detected, but there was nuchal rigidity, with the presence of the Kernig and Brudzinski signs.

A spinal puncture was immediately performed. The fluid obtained was purulent and thick. The first examination revealed gram-negative bacteria, but no tubercle bacilli. Examination of the blood showed 13,000 white cells, with 70 per cent polymorphonuclear neutrophils, 27 per cent lymphocytes, 3 per cent monocytes and no eosinophils. The urinalysis give normal results. The intracutaneous tuberculin test (Mantoux) gave a negative reaction. A roentgenogram of the chest revealed nothing abnormal.

Although sulfathiazole, 4 Gm. per twenty-four hours, was administered orally for two days, no improvement or aggravation of the patient's state was noted.

Since E. coli was identified on culture from the spinal fluid, streptomycin was given intramuscularly (0.1 Gm. [100,000 units] every three hours) and the same dose intrathecally once a day. The total daily dose of streptomycin was 0.9 Gm., or 900,000 units.

Improvement was shown from the third day of treatment, and by the ninth day symptoms of meningitis had disappeared entirely. However, a low grade fever (99.5 F.) continued to appear each evening. The duration of treatment with streptomycin was eighteen days, and the total amount of the drug given was 16 Gm.

It should be emphasized that the intrathecal administration of streptomycin was not always easy, the fluid being injected by drops with great difficulty. We were often obliged to inject sodium chloride solution into the cavity before proceeding with the injection of the streptomycin.

On April 25, a suboccipital puncture showed the fluid to be clear. The culture was negative for organisms. On April 27, the child left the hospital in good general health. Two months later we were informed that he was still quite healthy.

COMMENT

The daily amount of streptomycin given this child was greater than the dose we usually employ for patients with tuberculous meningitis. The duration of treatment for E. coli meningitis usually is not long, and we thought that we should give higher doses, considering that the total amount of streptomycin used would not exceed the patient's tolerance.

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METHEMOGLOBINEMIA IN INFANCY

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The purpose of this communication is to review the subject of methemoglobinemia in infancy and to add a report of a case of methemoglobinemia in neonatal life, resulting from the ingestion of well water containing large amounts of nitrates.

Methemoglobinemia has been recognized as a disease entity for many years. Several authors have grouped the cases according to the chemical responsible for the disturbance, such as aniline dyes (wax crayons), bismuth subnitrate, potassium chlorate, nitrites, acetanilid and sulfonamide compounds. Methemoglobinemia has also been reported to occur in the following clinical syndromes: congenital or idiopathic methemoglobinemia,[1] Winckel's disease [2] and enterogenous cyanosis.[3]

Interest in methemoglobinemia, as it occurs in infants, is only of recent date. In 1945, Comly [4] reported 2 cases of methemoglobinemia in early life and mentioned 19 others. He proposed that the high nitrate and nitrite content of well water used as a diluent for the formula was directly responsible for his cases. A total of at least 31 cases of methemoglobinemia of similar origin has been reported in the literature.

A summary of the important facts of the reported cases is given in table 1. All the infants were less than 90 days of age and were brought to a hospital from a rural community. In most instances the well water was boiled, excluding the probability of bacterial contamination. Clinically, the disease was manifested by one paramount sign, viz., cyanosis. This was the admitting complaint and its degree was usually out of proportion to other features. The cyanosis, which was progressive, affecting at first the lips and mouth and later the nail beds, skin of the distal portion of the extremities and the mucous membranes, came on approximately one month after the well water formula was begun. In several instances the blueness was intermittent. Frequently, gastrointestinal complaints,

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Presented at the combined meeting of the Rochester and Buffalo Pediatric Societies at Rochester, N. Y., Dec. 19, 1947.

1. Graybiel, A.; Lilienthal, J. L., and Riley, R. L.: Report of Case of Idiopathic Congenital Methemoglobinemia, Bull. Johns Hopkins Hosp. **76**:155-162 (April) 1945.

2. Feldman, W. M.: Case of So-Called Winckel's Disease (Cyanosis Afebrilis Icteria cum Hæmoglobinuria), Brit. J. Child. Dis. **24**:113-118 (April-June) 1927.

3. (*a*) Henstell, H. H., and Dameshek, W.: Enterogenous Cyanosis with Methemoglobinemia and Sulfhemoglobinemia: Spectro-Photometric Studies, J. Clin. Investigation **15**:464 (July) 1936. (*b*) Hijmans van den Bergh, A. A.: Enterogene Cyanose, Deutsches Arch. f. klin. Med. **83**:86-106 (May) 1905.

4. Comly, H. H.: Cyanosis from Nitrates in Well Water, J. A. M. A. **129**:112-116 (Sept. 8) 1945.

such as diarrhea and vomiting, were encountered. When the formula was temporarily discontinued because of these symptoms, the cyanosis lessened or disappeared, only to recur when the use of the milk mixture made with well water was resumed. Even when more pronounced symptoms occurred, such as restlessness, lethargy, apathy, air hunger and convulsions, examination of the child revealed a paucity of physical signs other than the slate gray blueness.

The usual laboratory aids were of little help in determining the cause of cyanosis. The concentration of hemoglobin was within the normal range. Roentgenologic study of the heart and lungs, culture of the blood and the electrocardiogram also failed to show anything unusual. Some babies had a leukocytosis.

TABLE 1.—*Cases of Methemoglobinemia Reported in the Literature*

Author	Age, Days	Symptoms Other Than Cyanosis	White Blood Cell Count	Methemoglobin Levels, % Methemoglobin	Well Water Analysis: Amount Ingested Per Day, Cc.	Well Water Analysis: Mg./Liter * Ingested NO₃	Well Water Analysis: Mg./Liter * Ingested NO₂	Well Water Analysis: Nitrogen NO₃	Well Water Analysis: P.P.M.† NO₂
Comly [4] (Iowa) ‡	27	Vomiting; diarrhea; apathy	6,750	1.5	540	619	0.33	140§	0.16¶
	33	Diarrhea; drowsiness	10,000	21.0	510	388	1.31	90	0.40
Ferrant [11] (Belgium)	35	Diarrhea; apathy	45,000	50.0	...	497	9.90	109	3.0
	30	Convulsions; died	28,000	¶	...	190	Trace	43	Trace
Fauscett and Miller [13] (Kansas)	18	Lethargy	22,700	58.0	600	66	Trace	15	Trace
	28 (Twins)	Lethargy	.....	71.0	600	66	Trace	15	Trace
	..	None	10,700	....	480	292	Trace	66	Trace
Medovoy, H. B.; Guest, W. C., and Victor, M.: Canad. M. A. J. 56: 503-508 (May) 1947 # (Canada)	35	Lethargy	.....	....	480	660 to 1,107	3.02	150 to 250	0.92
	44	Lethargy	.....	....	...	487	Trace	110	Trace
Larks (New York)	62	Vomiting; diarrhea	8,800	22	720	221	0.16	50	0.05

* X (mg. nitrate per liter) $= \frac{62}{14}$ p. p. m. of nitrate nitrogen.

† P. P. M. indicates parts per million of nitrate or nitrite nitrogen.

‡ Seventeen other cases are listed.

§ Normally no more than 1 p. p. m. of nitrate nitrogen.

‖ Normally no more than a trace of nitrite nitrogen per million parts.

¶ 0.1 mg. of nitrite per hundred cubic centimeters of blood.

Four other cases are listed.

Oxygen administered by tent, mask and catheter did not relieve the cyanosis. Improvement occurred slowly when the formula containing well water was discontinued and more promptly when methylthionine chloride U. S. P. (methylene blue) or vitamin C was administered. Of the reported cases of methemoglobinemia, death occurred in only 1.

REPORT OF A CASE

A 62 day old female infant was brought to the Children's Hospital, of Buffalo, from a farm in a nearby rural area. The complaint was persistent cyanosis of three days' duration. The family history was essentially noncontributory except for diabetes mellitus in the paternal grandparents. Other members of the household had no complaints or recent illness. (The mother had had mild toxemia in her last trimester of pregnancy.)

The child was a full term infant delivered spontaneously after a six hour labor with no neonatal abnormalities. The weight at birth was 7 pounds 7 ounces (3,373.6 Gm.).

The baby had been fed an artificial formula since birth. At the time of her admission the formula consisted of evaporated milk, 8 ounces (240 cc.), boiled water, 24 ounces (1,320 cc.), and a preparation containing calcium caseinate (casec®) 8 tablespoonfuls. The child received 4½ to 5 ounces (135 to 150 cc.) of this mixture five times a day. The water was obtained from an artesian well, piped directly into the house. This well was only a few feet from the house, and there were no apparent sources of contamination (no pigsty, latrine, barnyard or cesspool). Systemic inquiry obtained a history of occasional loose stools for the first five weeks of life. In the sixth week the child had four watery, nonbloody stools daily for several days, and for this reason the family physician substituted casec® for the corn syrup (karo®) which had been used in the formula since birth. For the next two weeks, until the time of her admission to the hospital, she had two normal stools per day.

The present illness began three days before her admission, when it was noted that the baby was blue about the mouth. This was attributed by the mother to a low room temperature. On the night before her admission the cyanosis became more intense and was evident in the nail beds and extremities. Nevertheless, the baby continued to take her feedings well. On awakening from her nap on the day of admission, she choked, gasped for air and vomited. She became very cyanotic for about five minutes, following which there was pronounced pallor. Cyanosis then returned but was less prominent.

The physical examination revealed a well developed, vigorous and well nourished 2 month old female infant in no acute distress. There was a slate gray cyanosis, particularly evident about the face, hands and feet. The rectal temperature was 98.6 F., the pulse rate 152, the respirations 28 and the weight 9 pounds 10 ounces (4,365.8 Gm.).

Course in the Hospital.—Because of the cyanosis the baby was placed under treatment with continuous oxygen inhalations, for two hours but without improvement. This fact, in addition to the paucity of physical findings and the history of well water ingestion, led to a provisional diagnosis of methemoglobinemia. Samples of blood for methemoglobin determinations were obtained eight hours after her admission. The cyanosis was still evident at this time, although somewhat diminished. Approximately fifteen hours after her admission another blood sample was obtained, following which 0.5 cc. of 1 per cent methylthionine chloride solution in 10 cc. of 10 per cent glucose solution was injected intravenously. This amounted to 1 mg. of methylthionine chloride per kilogram of body weight. Within an hour there was perceptible improvement in the color. Two other blood samples were subsequently obtained (see table 2). Four hours following the injection of the methylthionine chloride solution the cyanosis had completely disappeared. The patient continued to do well, took her formula, had normal stools and was vigorous. She was discharged to her home on the fourth day from the hospital. The parents were advised to use another source of water which was known to be free of excessive amounts of nitrates and nitrites.

Laboratory Findings.—The electrocardiogram showed a normal record. The roentgenogram revealed clear lungs and a normal heart; the diaphragm was normally situated, and there was no evidence of an enlarged thymus. Blood culture showed no growth in four days. Cultures of material from the nasopharynx and throat grew many hemolytic staphylococci (aureus) and pneumococci. A stool culture yielded a strain of Escherichia coli which produced large amounts of nitrite in twenty-four hours. The nonprotein nitrogen level in the blood was

58 mg. per hundred cubic centimeters initially, and after three days it was down to 39 mg. The carbon dioxide—combining power of the blood was 22 milliequivalents (49 volumes per cent). The hemoglobin content of the blood was 12 Gm. per hundred cubic centimeters; there were 8,800 white blood cells, with 33 per cent filamented forms, 64 per cent lymphocytes, 1 per cent eosinophils, and 1 per cent monocytes. On the day of her discharge the hemoglobin content was 13.5 Gm. per hundred cubic centimeters and 9,400 white blood cells, with 15 per cent filamented forms, 81 per cent lymphocytes, and 1 per cent monocytes.

Methemoglobin determinations were performed on whole blood to which 1 to 2 mg. of a mixture of an oxalate and a fluoride was added,[5] the final reading being obtained on a Beckman spectrophotometer (table 2). Chemical and bacteriologic analyses of the well water on two different days were made. There were

TABLE 2.—*Results of Spectrophotometric Determinations**

Number of Hours After Admission	Methemoglobin Levels, Percentage of Total Hemoglobin
6	22
15	18
16 (1 hour after administration of methylthionine chloride)	4.9
30 (15 hours after administration of methylthionine chloride)	0.0

* Determinations were made by Dr. Wilson Langley, of the Department of Biochemistry, University of Buffalo School of Medicine, Buffalo, with use of the method of Michel and Harris.[5]

TABLE 3.—*Analyses of Well Water**

	Well No. 1, Used for Formula	Well No. 2
Chemical †		
Nitrate nitrogen, p.p.m.	80	0.1
Nitrite nitrogen, p.p.m.	0.05	0.25
Bacteriologic		
Agar count (coliform group), colonies in 24 hours	1,900 per cc.	...

* Two specimens.
† Chemical analysis was made by Dr. Barton F. Hauenstein, Health Department of Erie County, N. Y.

two wells on the farm and samples were obtained from both. From these studies one can conclude that the water in the formula contained large amounts of nitrate, although the source of this contamination could not be ascertained (table 3).

COMMENT

Comly[4] suggested that the nitrates ingested in large amounts are converted to nitrites and then absorbed from the intestine. Bacteria present in the intestinal flora, or even in well water, are capable of transforming the nitrates to nitrites. Such organisms are numerous, for E. coli, Streptococcus viridans, pneumococci and others form nitrite readily.[6] On entrance into the circulation, nitrite oxidizes

5. Michel, H. O., and Harris, J. S.: Blood Pigments, J. Lab. & Clin. Med. **25**:445-463 (Feb.) 1940.

6. Zobell, C. E., and Meyer, K. F.: Factors Influencing the Reduction of Nitrates by Bacteria in Semisolid Media, J. Bact. **24**:273-281 (Oct.) 1932.

the ferrous form of hemoglobin to the ferric form with the production of methemoglobin. Hijmans van den Bergh [2b] expressed the belief that the normal mucous membrane of the intestine acts as a barrier to the absorption of nitrite. Disturbance of the mucous membrane of the intestine during diarrheal episodes may allow this chemical to be readily absorbed.

The question has been raised as to the reason methemoglobinemia occurs so readily in infants and less readily in older children and adults. Three possible answers come to mind: 1. The difference may be due primarily to the quantitative ingestion of nitrites or nitrates, for the amount of water ingested per kilogram of body weight in early life is much greater than later on—a 60 Kg. male would have to consume six times his usual water intake if his intake were to be comparable with that of a small infant. This is particularly true of those infants fed on evaporated milk formulas. 2. The species of nitrite-forming bacteria, as well as their number in the intestinal tract, would also be a factor in the total amount of nitrite available for absorption (see addendum). 3. The ease of development of methemoglobinemia may depend on qualitative differences in the hemoglobin of the infant and adult. Chemical,[7] physicochemical,[8] immunologic [9] and other distinctions [10] are known to exist between these two hemoglobins.

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7. Koerber, E.: Ueber Differenzen des Bluffarbstoffs, Inaug. Dissert., Dorpat, 1866; cited by Ziemke, E.: Ueber die ungleiche Resistenz des Blutfarbstoffes verschiedener Thiere gegen Alkalien und eine hierauf gegründete Methode zur Unterschiedung von Menschen- und Thierblut, Vrtljschr. f. gerichtl. Med. **22**:77-103, 1901. Brinkman, R., and Jonxis, J. H. P.: Alkaline Resistance and Spreading Velocity of Foetal Types of Mammalian Hemoglobin, J. Physiol. **88**:162-166 (Nov. 6) 1936. Bischoff, H., and Schulte, H.: Further Studies on Hemoglobin Resistance in Infants, Jahrb. f. Kinderh. **112**:56-61 (March) 1926. Jongbloed, J.: Spectrophotometer Investigation in Differences Between Foetal and Maternal Hæmoglobin in Man, J. Physiol. **92**:229-231 (April 14) 1938. Trought, H.: The Specificity of Hemoglobins Including Embryonic Hemoglobin, Arch. Dis. Childhood **7**:259-262 (Oct.) 1932.

8. Barcroft, J.: Conditions of Foetal Respiration, Lancet **2**:1021-1024 (Nov. 4) 1933. Eastman, N. J.; Geiling, E. M. K., and De Lawder, A. M.: Foetal Blood Studies: Oxygen and Carbon-Dioxide Dissociation Curves of Foetal Blood, Bull. Johns Hopkins Hosp. **53**:246-254 (Nov.) 1933. Darling, R. C.; Smith, C.; Asmussen, E., and Cohen, F.: Some Properties of Human and Foetal Hemoglobin, J. Clin. Investigation **20**:739-747 (Nov.) 1941. Darling, R. C., and Roughton, F. J. W.: The Effect of Methemoglobin on the Equilibrium Between Oxygen and Hemoglobin, Am. J. Physiol. **137**:56-68 (Aug.) 1942.

9. Darrow, R. R.; Mowakovsky, S., and Austin, M. H.: Specificity of Foetal and Adult Hemoglobin Precipitins, Arch. Path. **30**:873-880 (Oct.) 1940. Hektoen, L., and Schulhoff, K.: Is Antigenic Action of Hemoglobin Due to Globin? J. Infect. Dis. **41**:476-478 (Dec.) 1927.

10. Andersch, M. A.; Wilson, D. A., and Menten, M. A.: Sedimentation Constants of Electrophoretic Mobilities of Adult and Foetal Hemoglobin, J. Biol. Chem. **153**:301-305 (April) 1944. Schenck, E. G.: Untersuchungen über das Globin bei Tieren, gesunden und kranken Menschen: Ein Bitrag zur Kenntnis der dynamischen Konstitution des Hämoglobin, Arch. f. exper. Path. u. Pharmakol. **150**:160-172, 1930. Haurowitz, F.: Die Hæmoglobine des Menschen, Ztschr. f. physiol. Chem. **232**:125-145, 1935; Zur Chemie des Blutfarbstoffes: Ueber die Spezifitaet der Haemoglobine und die von Kruegersche Reaktion, ibid. **183**:78-87, 1929. Josephs, H. W.: Urobilin Excretion of Infancy and Childhood: Relation to Blood Formation, Bull. Johns Hopkins Hosp. **55**:154-168 (Aug.) 1934.

The amounts of nitrate ingested per liter by the infants reviewed are summarized in table 1. Despite the evidence of methemoglobinemia in all these infants, the quantities of nitrate ingested varied considerably (66 to 1,107 mg. per liter). For example, 1 of the patients, a 20 day old infant, whose nitrate intake was only 66 mg. of nitrate ion per liter, had an extremely high methemoglobin level in the blood (70 per cent). Ferrant,[11] in one of his fatal cases, could find only minute amounts (0.1 mg. per hundred cubic centimeters) of nitrite in the blood, despite the extreme state of cyanosis. Faucett and Miller[12] stated that in the household where they detected methemoglobinemia in a 2 month old infant another 6 month old baby living in this home did not become cyanotic or develop any symptoms of intoxication when given similar quantities of well water. In conjunction with the aforementioned observations made on the present patient, an attempt was made to study the rapidity of formation of methemoglobin in vitro by the use of nitrites. Preliminary experiments, as yet inconclusive, seem to indicate that nitrite forms methemoglobin more quickly with fetal hemoglobin than with adult hemoglobin.[13] The age of the patient, perhaps, is one of the determining factors in the ease of formation of methemoglobinemia. It seems unlikely, therefore, that the symptoms are entirely dependent on the amount of nitrite ingested.

Methylthionine chloride has been used in the treatment of methemoglobinemia for many years. The mechanism of its action, however, is not completely understood. Several authors have stated the opinion that it oxidizes the ferric form of iron in the hemoglobin to the ferrous.[14] Perhaps its action is on one of the enzyme systems, for Gutman and his co-workers[15] and others[16] have shown that an equilibrium exists between oxyhemoglobin, hemoglobin (ferrous iron) and methemoglobin (ferric iron) which is dependent on a glycolytic process. Other chemicals can influence the system, depending on the site of action, either accelerating or inhibiting the conversion of methemoglobin to hemoglobin. Ascorbic acid has also been used for the treatment of methemoglobinemia, but the time required for its action is longer than that needed for methylthionine chloride.[17]

SUMMARY

A case of methemoglobinemia in a 62 day old infant is presented. The history revealed that well water containing large amounts of nitrate had been ingested.

11. Ferrant, M.: Methemoglobinemia, J. Pediat. **29**:585-592 (Nov.) 1946.

12. Faucett, R. L., and Miller, H. C.: Methemoglobinemia Occurring in Infants Fed Milk Diluted with Well Water of High Nitrate Content, J. Pediat. **29**:593-596 (Nov.) 1946.

13. The method used and the results obtained are to be published.

14. Wendel, W. B.: The Control of Methemoglobinemia with Methylene Blue, J. Clin. Investigation **18**:179-185 (May 4) 1939.

15. Gutman, H. R.; Jandorf, B. J., and Bodansky, O.: Role of Pyridine Nucleotides in Reduction of Methemoglobin, J. Biol. Chem. **169**:145-152 (June) 1947.

16. Drabkin, D. L.: Hemoglobin, Glucose, Oxygen and Water in Erythrocyte: Concept of Biological Magnitudes, Based upon Molecular Dimensions, Science, **101**:445-451 (May 4) 1945; Maintenance of Active Hemoglobin—Function of Erythrocytes, Federation Proc. **5**:132 (March) 1946.

17. Carnrick, M.; Polis, B. D., and Klein, T.: Methemoglobin Treatment with Ascorbic Acid, Arch. Int. Med. **78**:293-303 (Sept.) 1946. Finch, C. A.: Methemoglobinemia and Sulfhemoglobinemia, New England J. Med. **239**:470-478 (Sept. 23) 1948.

There was severe cyanosis which was quickly relieved by administration of methylthionine chloride. A brief review of the literature is given.

When cyanosis occurs in a baby living in a rural community with a history of ingestion of well water, methemoglobinemia should be excluded as a cause for the cyanosis.

It is proposed that the difference in the rate of formation of methemoglobin in infants and in persons in later life may be based on a qualitative difference between their hemoglobins.

ADDENDUM

Since this paper was first presented, several additional reports have appeared in the literature pertaining to methemoglobinemia in young infants following ingestion of well water containing large amounts of nitrates. For the most part they were case studies and were of interest in that all the affected infants were less than 3 months of age and the amount of nitrate ingested per liter per day ranged from 600 to 4,300 mg.[18] The most important paper was that of Cornblath and Hartmann.[19] These authors proposed that small infants are more susceptible to methemoglobinemia from the ingestion of well water containing large amounts of nitrates because of the gastric hypoacidity frequently found in the neonatal period. This allows the nitrite-forming bacteria usually found in the colon to flourish high in the gastrointestinal tract. The infant, therefore, has a greater amount ot nitrite available for absorption and the formation of methemoglobin.

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18. Chapin, F. J.: Methemoglobinemia from Nitrates in Well Water, J. Michigan M. Soc. **46**:938 (Aug.) 1947. Stafford, G. E.: Methemoglobinemia in Infants from Well Water Containing High Concentrations of Nitrates, Nebraska M. J. **32**:392-394 (Oct.) 1947. Woolley, P. V., Jr.: Methemoglobinemia Due to Well Water (Conference at the Children's Hospital of Michigan), J. Pediat. **33**:506-507 (Oct.) 1948.

19. Cornblath, M., and Hartmann, A. F.: Methemoglobinemia in Young Infants, J. Pediat. **33**:421-425 (Oct.) 1948.

Progress in Pediatrics

CEREBRAL PALSY

Selection and Training of the Child with Normal Mentality

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CEREBRAL palsy, formerly known as spastic paralysis, is now recognized as the greatest consistent cause of crippling in childhood. Poliomyelitis still ruthlessly ravages the nation's children. However, with the tremendous resources available for diagnosis of, research on, and training and treatment for, poliomyelitis permanent deformities are now of milder degree. Cerebral palsy alone remains the great crippler of children, persistent in its ratio to the population and disregarding all economic, geographic, social, racial and educational boundaries. Handicaps due to cerebral palsy remain the most neglected group of handicaps in this era of great advance in preservation and rehabilitation of the stricken child. Public opinion, aroused parents and our own medical conscience remind us that to let live but to refuse to rehabilitate is not our way of life. Since the epochal studies of McIntire,[1] who proved beyond doubt that at least two thirds of children having cerebral palsy had normal intelligence and were, therefore, definitely educable, our responsibility to rehabilitate these forgotten children has been singularly clear.

NATURE OF CEREBRAL PALSY

To rehabilitate these children, one must obviously possess a clear understanding of the nature of this complex clinical entity. What, then, is cerebral palsy? Cerebral palsy is a general term used to designate any paralysis, weakness, incoordination or functional deviation of the motor system resulting from an intracranial lesion. Since the brain is the center not only of muscular control but also of intelligence, behavior control, personality and many other functions, it is possible for brain injury to result in motor paralysis or convulsions, mental deficiency, personality problems or sensory defects, such as loss of hearing, vision or

Read by invitation at the annual meeting of the American Academy of Pediatrics, New Jersey Fellows, Newark, N. J., Jan. 26, 1949.

1. McIntire, J. T.: Incidence of Feeblemindedness in the Cerebral Palsied, Am. J. Ment. Deficiency **43**:2 and 44, 1938.

sense of touch, depending on the location and the degree of involvement. The physical symptoms are generally far more obvious clinically than the mental, emotional and other associated handicaps.

Phelps [2] divided the cerebral palsy group into five distinct clinical types based primarily on the kind of motor handicap: (1) true cerebral spastic paralysis (20 per cent), (2) athetosis (40 per cent), (3) rigidity (20 per cent), (4) ataxia (10 per cent) and (5) tremor (5 per cent). This classification is based on the outstanding clinical manifestations displayed by the patient. In the child with true spasticity, the characteristic signs are hyperirritability, hypercontractility and hypertonia of the muscles involved. These muscles exhibit the physiologic phenomenon described by Liddell and Sherrington [3] as the "stretch reflex," in which contraction of the antagonist muscle, for example, the hamstring muscles in flexing the knee joint, produces stretching of the hypercontractile muscle, the quadriceps in this case, causing it to contract and block the voluntary motion to flex the knee. The quadriceps is then said to be spastic. The deep tendon reflexes are hyperactive and clonus may be present, the clonus representing an exaggeration of the stretch reflex. Because of the location of the lesion, usually involving both areas 4 and 6 (Fulton [4]) of the motor cortex, one may observe a combination of muscular dysfunction, with spastic muscles, flaccid muscles and normal muscles in the same patient. This combined dysfunction causes the imbalance of muscle power which handicaps the spastic child.

The athetoid child differs in that his handicap is due to involuntary motions of no constant pattern which attempt to move joints rather than individual muscles. The pathologic change here is in the cells of the basal ganglions of the midbrain, the putamen, caudate nucleus and tegmental nucleus, which results in the abnormal release of impulses from the motor cortex. The braking mechanism for this steady stream of impulses from the motor cortex fails and involuntary movements occur —rapid or slow, constant or intermittent—which usually disappear during sleep. The constant grimacing and facial distortion of the athetoid child has, in the past, led to an incorrect diagnosis of mental retardation.

The ataxic children show a disturbance or loss of kinesthetic sense and balance. They walk with a wide base and have considerable muscular hypotonicity which retards walking activity. Speech may be thick and dragging. There is often an associated nystagmus. The possibility for

2. Phelps, W. M.: The Differential Characteristics of Spasticity and Athetosis in Relation to Therapeutic Measures, New York State J. Med. 41:1287, 1941.

3. Liddell, E. G. T., and Sherrington, C.: Reflexes in Response to Stretch (Myostatic Reflexes), Proc. Roy. Soc., London s.I 98:212, 1924-1925.

4. Fulton, J. F.: Physiology of the Nervous System, London, Oxford University Press, 1938.

spontaneous improvement is better in children of this group than in those with any other type of cerebral palsy.

The "rigid" child presents a loss of tonus or elasticity in muscles, which give a "plastic" or "lead pipe" response to passive motions of a joint. There is no true stretch reflex in the muscles. The rigidity may be intermittent or constant. Because of the lesion therein, namely, multiple petechial hemorrhages in the cerebral cortex, the incidence of mental retardation in this group is high.

Tremors may be of the intention or of the nonintention type and are characterized by involuntary motions which are reciprocal in nature and regular in rhythm. The lesion is usually a hemorrhage in the tegmental nucleus or in other elements of the basal ganglions.

ETIOLOGIC FACTORS

What are the factors which may cause these various aberrations of the motor system? Since 1862, when Little [5] described a microcephalic idiot with spastic diplegia, trauma during birth has been considered the principal etiologic agent. Modern statistics, such as those of Ford [6] ascribing 6 per cent and those of Phelps attributing only 3 per cent of all cerebral palsy to birth trauma, belie the unfortunate onus placed on the obstetrician.

Defective prenatal development is the commonest offender, especially in the ataxic and athetoid child. Other important prenatal factors are: (1) rubella during first trimester of pregnancy, (2) the toxemias of pregnancy, (3) premature separation of the placenta and (4) endocrine dysfunction. When there is symmetry of involvement, such as bilaterally equal involvement of arms or legs, one should suspect a prenatal background. In fact, often congenital athetosis may cause a most difficult labor—although the postnatal physical handicap may be attributed falsely to the difficult labor.

The group of so-called birth injuries are usually of two types: those resulting from direct mechanical injury and those following prolonged anoxia. Mechanical injury may be due to incorrect application of forceps, failure to apply forceps in protracted labor, excessive traction on the head and, most important, prematurity. Here, the intracranial birth hemorrhage is due to the rupture of the delicate blood vessels by the sudden drop from the intrauterine pressure to the atmospheric pressure during a precipitous delivery. This hemorrhage is usually a

5. Little, J.: On the Influence of Abnormal Parturition, Difficult Labour, Premature Births and Asphyxia Neonatorum on the Mental and Physical Condition of the Child Especially in Relation to Deformities, Tr. Obst. Soc. London **3**:293, 1861.

6. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood and Adolescence, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1946.

small one in the vertex of the brain beneath the anterior fontanel producing the characteristic spastic diplegia. Cerebral anoxia is a frequent causal factor—the injudicious use of analgesic and anesthetic agents in the second stage of labor, passive congestion of the brain as a result of the umbilical cord's being wrapped around the neck of the fetus or a short period of fetal apnea will produce anoxia of the brain and intercellular damage.

In the postnatal group of injuries, severe jaundice occurring during the first weeks of life associated with erythroblastosis fetalis and disturbances of the Rh factor will frequently result in damage to the basal ganglions, with the development of athetosis. Fractures of the skull with cortical damage, severe convulsive seizures, whooping cough and postexanthematous encephalitis are other common offenders in the production of cerebral palsy.

TREATMENT AND REHABILITATION

With proper treatment and training, children with cerebral palsy can and do improve physically, mentally and socially. The actual damage to nerve tissue, of course, is irreversible and permanent. The proof of the surprising capacity of these children for improvement was first demonstrated in New Jersey by Phelps and McIntire at the Babbitt Hospital in Vineland more than ten years ago. Twenty boys of normal mentality from 5 to 15 years of age having cerebral palsy were given a medically prescribed and supervised course of treatment for almost six years. On entrance to the hospital only 30 per cent of these children were capable of attending regular public schools. On discharge, this proportion had grown to the amazing figure of 77 per cent. The rate of social maturation of these children was about three times as rapid after the course of training as it was before. The proof of this experiment has now been repeated in almost every corner of the country, in outpatient clinics, as well as in hospital-school units.

The first step in the rehabilitation of the child with cerebral palsy, as with any patient, is an accurate diagnosis. The child must be classified according to the type of cerebral palsy he has and his neuromuscular picture evaluated. In addition to involvement of the extremities, defects of speech, hearing and vision must be assessed. In some surveys of children with cerebral palsy, 60 per cent had associated speech defects. Speech defects in the spastic child are due primarily to spasticity of the muscles of the larynx, pharynx, tongue and lips. In the athetoid patients, involuntary movements of the diaphragm, which interfere with breath control, add to the speech handicap. Hearing defects, especially in the athetoid child, are often selective impairments for certain ranges of pitch—the *s*, *t*, *th* and *f* sounds—and require special management. Visual defects include not only abnormal vision but loss of control of the

extraocular muscles, resulting in convergent squints and nystagmus. Seizures of both the grand and the petit mal types occur more frequently in these patients than in the normal child and must be controlled effectively.

Coincident with the physical assessment, the mental ability of the child must be evaluated. The procedure is fraught with many possibilities of error for the child. Satisfactory testing with standard tests is of value only when the psychologist knows in advance the motor, speech, visual and hearing handicaps of the child. Most of the tests for grading intelligence assume that a normal motor mechanism exists and the score depends, for the most part, on the rapidity of the motor response and the communication facilities. To try to evaluate the mental ability of a child who has no method of rapid response, who is unable to talk, write or use his hands in any coordinated manner, is a difficult task. It is no wonder, then, that until recently all children with cerebral palsy were considered mentally retarded. In addition to the lack of speech and motor coordination, these children suffer from the lack of environmental stimulation necessary to normal mental development—this holds true for all "shut-in" or homebound children. These children are spoken of as being "feebleminded by deprivation." The social maturation level and the emotional background of the child must also be evaluated by the psychologist to complete his observations.

The first task, then, in the rehabilitation of the child with cerebral palsy is that of evaluation. Each child is an individual problem, and the problems occur in infinite variations. It is only after these preliminary screenings, wherein the clinical diagnosis, neuromuscular picture, assessment of associated handicaps and psychologic examinations are completed, that one can map out a plan of treatment. The routine aims of treatment in all rehabilitation of children having cerebral palsy revolve about four main objectives: (1) locomotion, (2) speech, (3) self help (arm skills) and (4) education.

The first objective, in general, is to teach the child to walk. Braces are used to support the weak muscles (as in poliomyelitis), to prevent contractures and, chiefly, to overcome the pull of undesired muscle contractions or joint motions. Many of these children have no concept whatever of the walking process—often it takes months to train them in this pattern of putting one leg in front of the other. It is done by conditioning excercises, much as in learning to play the piano. Once the automatic phase is learned, the child is trained to improvise—to walk without his braces or crutches. These technics are carried out by highly trained physical therapists much as muscle reeducation is done in the modern treatment for patients with poliomyelitis. A variety of equipment is available to help the child achieve the ultimate goal of walking independently without support. The method of training is patterned

after the maturation process of the normal child, who usually pulls himself up at 3 to 6 months, sits up at 6 months, crawls at 9 months, walks at 12 months and talks at approximately 18 months. This pattern is followed by training the child first to sit, then to kneel, then to stand and, finally, to walk.

Occupational therapists teach the children the skilled arm and hand movements necessary for feeding, dressing and general self sufficiency. Speech therapy is in the hands of specially trained therapists who have a most difficult task in training the muscles of the diaphragm, tongue, larynx, pharynx and lips.

Surgical procedures on the brain and spinal cord have not proved to be of any over-all general help. Surgical treatment of the extremities is of limited value in selected cases and its use is generally reserved for late adolescence when maximum bony growth has been achieved. Many contractures can be avoided by the wearing of simple day or night braces. Drugs, like neostigmine, atropine, curare and mephenesin (tolserol®) are of assistance only as adjuvants to the physical therapy. What is required is intensive practice, sheer perseverence and sympathetic training in skilled hands.

Every child with cerebral palsy of normal intelligence is entitled to an academic education. A large percentage of these children go to regular public schools—one has seen the hemiplegic children and some of those with the milder athetoid and spastic paralyses in the regular schools. They can hold their own well. It is most important that the field of special education be widened so that more teachers are available who possess special knowledge of teaching methods for the handicapped child. Special schools for handicapped children—clinic schools and hospital schools—must be established for the children with cerebral palsy of normal intelligence.

The blame for neglect, past and present, rests to a great extent on the physician's doorstep. The tragedy of the neglect of these children is not in those who are feebleminded but in that large majority of normal or of superior intelligence—sensitive children, possessed of normal ambitions, desires and capacity for affection. Our way of life is to do our utmost to restore these children to their rightful places in society.

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Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

THIOUREA AND THE INHIBITION OF GROWTH OF FUNGI. T. S. DANOWSKI and M. TAGER, J. Infect. Dis. **82**:119 (March-April) 1948.

Thiourea suppressed in a varying degree the in vitro growth of several pathogenic fungi. The presence of blood or serum minimized this action. Ultrafiltrate of serum, spinal fluid and urine interfered less notably with the action of the thiourea. Thiourea failed to influence the course of torulosis and of blastomycosis induced in mice.

FROM THE AUTHORS' SUMMARY.

INHIBITION OF THE GROWTH OF FUNGI BY THIOUREA DERIVATIVES, PARTICULARLY HYDRAZINE DITHIOCARBAMYL. M. TAGER and T. S. DANOWSKI, J. Infect. Dis. **82**:126 (March-April) 1948.

Of a series of thiourea derivatives tested in vitro against Cryptococcus hominis, dithiocarbamyl hydrazine and thiocarbamyl hydrazine suppressed growth in the presence of serum. Dithiocarbamyl hydrazine effectively inhibited the growth of 9 of 15 pathogenic fungi in mediums with and without added serum. It failed to influence favorably the course of blastomycosis and of torulosis induced in mice; its administration was associated with some toxic manifestations. Thiocarbamyl hydrazine, though effective in vitro, was unstable in aqueous solution and highly toxic to mice.

FROM THE AUTHORS' SUMMARY.

STREPTOCOCCAL HYALURONIC ACID AND HYALURONIDASE: I. HYALURONIDASE ACTIVITY OF NONCAPSULATED GROUP A STREPTOCOCCI. ROBERT M. PIKE, J. Infect. Dis. **83**:1 (July-Aug.) 1948.

A test was described which indicates the effect of growing cultures on hyaluronic acid included in the culture medium. By means of this test, 55 per cent of 110 strains of noncapsulated group A streptococci were shown to reduce the hyaluronic acid content of the medium significantly in twenty-four hours. On prolongation of the incubation to several days, additional strains were discovered to be producers of hyaluronidase. The turbidimetric measurements of hyaluronidase activity appear to be practical for the detection of small amounts of the enzyme.

FROM THE AUTHOR'S SUMMARY.

STREPTOCOCCAL HYALURONIC ACID AND HYALURONIDASE: II. PRODUCTION AND SUBSEQUENT DESTRUCTION OF HYALURONIC ACID BY CERTAIN STRAINS OF GROUP A STREPTOCOCCI. ROBERT M. PIKE, J. Infect. Dis. **83**:12 (July-Aug.) 1948.

Continued incubation of broth cultures of several strains of mucoid group A streptococci resulted in the disappearance of the capsular polysaccharide from the culture fluid. The reduction in the concentration of hyaluronic acid also occurred in sterile filtrates and was prevented by heating at 60 C. (140 F.). Strains which destroyed their own hyaluronic acid also destroyed the hyaluronic acid produced by another strain. It was concluded that certain mucoid strains produce hyaluronidase but that the activity of the enzyme is relatively weak and variable.

FROM THE AUTHOR'S SUMMARY.

STREPTOCOCCAL HYALURONIC ACID AND HYALURONIDASE: III. VIRULENCE OF GROUP A STREPTOCOCCI FOR MICE IN RELATION TO THE PRODUCTION AND DESTRUCTION OF HYALURONIC ACID. ROBERT M. PIKE, J. Infect. Dis. **83**:19 (July-Aug.) 1948.

Mouse passage of 10 strains of capsulated group A streptococci resulted in a substantial increase in the virulence of 7 strains for mice. There was no comparable or consistent increase, however, in the amount of hyaluronic acid produced in broth cultures. No quantitative relationship between the amount of hyaluronic acid produced in broth and the virulence for mice was evident either before or after mouse passage.

FROM THE AUTHOR'S SUMMARY.

STUDIES WITH SHIGELLA DYSENTERIAE (SHIGA): II. THE EFFECT OF SERUMS ON EXPERIMENTAL INFECTION AND INTOXICATION IN MICE. SARA E. BRANHAM and SADIE A. CARLIN, J. Infect. Dis. **83**:66 (July-Aug.) 1948.

Whole serum prepared by immunization of horses with culture suspensions, is usually polyvalent and is primarily antibacterial in action, though some antitoxin, usually not over 500 units per cubic centimeter, is present. Monovalent Shiga antitoxin, prepared by immunization of horses with bacteria-free toxins, usually concentrated and refined, has, as a rule, from 2,500 to 5,000 units per cubic centimeter.

There is no doubt that results obtained with mice cannot be arbitrarily substituted for human clinical data, especially when the infections and intoxications are produced experimentally by parenteral injection. However, in the absence of reports on the use of the serums in human beings, studies on these animals give some information about the agents and their action and may have value in indicating what may be expected from them under certain conditions.

Antibacterial serums are of definite therapeutic value in mice if given early enough in the course of infection; the earlier a serum is given, the smaller the amount required. Shiga antitoxin, even of high titer, was observed to be a poor therapeutic agent in experimental infections. These experimental infections in mice differ in many ways from spontaneous infection in man, and conclusions concerning the place of antitoxin and antibacterial serum in treatment cannot be drawn too hastily.

TOOMEY, Cleveland.

OLIGODYNAMIC ACTION OF METALLIC ELEMENTS AND OF METAL ALLOYS ON CERTAIN BACTERIA AND VIRUSES. CHARLES F. MCKHANN, HARVE J. CARLSON and HARRIET DOUGLAS, Pediatrics **2**:272 (Sept.) 1948.

Results of reinvestigation of the inhibitory effects of metallic elements on bacteria and fungi confirmed and extended earlier observations in this field. Additional studies on the virus of influenza indicated significant effects in destruction or reduction of infectivity of the virus by contact with brass, osmium and rhenium, with lesser effect exerted by other metals. Only one element, rhenium, could be interpreted to have any effect on poliomyelitis virus.

FROM THE AUTHORS' SUMMARY.

Metabolism; Infant Feeding; Milk and Other Foods

MARGARINE AND THE GROWTH OF CHILDREN. HARRY LEICHENGER, GEORGE EISENBERG and ANTON J. CARLSON, J. A. M. A. **136**:388 (Feb. 7) 1948.

One hundred and sixty children from 3 to 16 years of age, half of whom were orphaned or from broken homes, living in one institution, were fed a diet so regulated that 25 to 30 per cent of the total calories was supplied by fat. Margarine

fortified with vitamin A constituted 65 to 70 per cent of the fat calories. One hundred and five children in an approximately similar institution were given butter in the same amounts. During the two years of the study there was no appreciable difference between the two groups in gain in weight and height, in the blood count or in the amount of illness, which was only slight.

KIMBALL, Evanston, Ill.

A STUDY OF AN ENRICHED CEREAL IN CHILD FEEDING. CHARLES URBACH, PAULINE BERRY MACK and JOSEPH STOKES JR., Pediatrics **1**:70 (Jan.) 1948.

In a study of the value of adding a daily portion of enriched cereal (together with a standard amount of sugar and whole milk) to the school-feeding program of undernourished grade school children whose home dietaries were poor, and whose regular school lunches did not compensate for the inadequate home dietaries, three approximately matched groups during two successive years were fed, respectively, the enriched cereal, an equivalent amount calorically of common farina and no cereal at school. The feeding program lasted for seven months during each school year.

The enriched cereal was superior to the common farina in percentage of protein, and the protein was of a predigested type. It was enriched with calcium, phosphorus, iron, copper, thiamine, riboflavin, nicotinic acid and pantothenic acid.

Hematologic values decreased, or showed little or no improvement, in all groups during both years of the study.

The first two groups were superior to the third in gain in weight, in decrease in blood phosphatase during both years and in the condition of the tongue and showed an increase in urinary thiamine during the second year. Only the group given enriched cereal showed improvement in these last two respects during the first year.

The group given enriched cereal was superior to both the other groups both years in the increase of vitamin A and ascorbic acid in the blood plasma. This occurred in spite of the fact that the enriched cereal did not contain these nutrients and that the three experimental groups were closely similar in intake of vitamin A and ascorbic acid at home and at school.

The group given enriched cereal, further, was superior to both other groups in the following respects: increase in urinary output of riboflavin, improvement in skeletal maturity, improvement in skeletal mineralization, recession in dental caries, recession of corneal vascularization and condition of the gums.

None of the personnel, the pediatrician, the dental examiner, the person evaluating roentgenograms for skeletal maturity, and the medical assistant making the biomicroscopic examinations, knew the experimental groups into which the children were placed.

FROM THE AUTHORS' SUMMARY.

THE INCIDENCE OF BREAST FEEDING IN HOSPITALS IN THE UNITED STATES. KATHERIN BAIN, Pediatrics **2**:313 (Sept.) 1948.

The data presented, obtained in the Study of Child Health Services of the American Academy of Pediatrics, are the first national figures on the incidence of breast feeding in hospitals in the United States.

A one week record of the type of feeding of all infants discharged alive (under 8 days and 8 days of age and over) from the nursery for the newborn was supplied by 72 per cent of the 3,500 hospitals of 25 or more beds which admitted women for delivery. The sample was representative of hospitals in all regions and in rural and urban areas and of hospitals of all sizes.

The type of feeding at time of discharge was reported for 39,171 infants. One third were given the bottle only at the time of discharge, two thirds being fed by breast only or fed by breast and bottle. The proportion entirely weaned at time of discharge was less in areas away from metropolitan centers and less in small and large, as compared with medium-sized (100 to 249 beds), hospitals.

There are wide regional differences in the incidence of breast feeding. In the Northeast region, 61 per cent of the infants were being given artificial feeding on discharge, as compared with 18 per cent in the South and Southwest. The states in which the proportion of infants entirely artificially fed exceeded 50 per cent were all in the Northeast area. The states with the highest incidence were Connecticut and New Hampshire with 70 and 72 per cent. The states with the lowest incidence of bottle feeding were South Carolina and Alabama with 10 and 11 per cent, respectively.

The group of infants discharged from the hospital under 8 days of age had a higher incidence of breast feeding than that which remained eight days or longer.

FROM THE AUTHOR'S SUMMARY.

GALACTOSE STUDIES IN AN INFANT WITH IDIOPATHIC GALACTOSE INTOLERANCE. LAWRENCE GREENMAN and JOHN C. RATHBUN, Pediatrics **2**:666 (Dec.) 1948.

Galactose metabolism was studied in 5 convalescent infants and in 1 patient with idiopathic galactosuria, hepatomegaly, splenomegaly and cataracts. Concentrations of galactose in the venous blood and the degree of galactosuria were determined at intervals following rapid intravenous injection of a 50 per cent solution of sugar in water at doses of 1.2 Gm. per kilogram of body weight. Galactose tolerance of convalescent infants was similar to that of healthy adults. The patient with idiopathic galactosuria, however, despite clinical improvement on a galactose-free diet, had persistent intolerance to the sugar, with seventy-five minute blood levels averaging 164 mg. per hundred cubic centimeters in contrast to 13 mg. per hundred cubic centimeters in convalescent infants. Simultaneous administration of glucose, 1 to 2 Gm. per kilogram of body weight, or insulin, 2 units subcutaneously, with the galactose, accelerated the rate of disposal of the latter partially, but not completely, toward normal. Galactosemia at seventy-five minutes was 42 to 65 mg. per hundred cubic centimeters less than in the control studies on the patient, and galactosuria was concomitantly reduced. Administration of alcohol did not alter the patient's galactose tolerance. This suggests that, in addition to restriction of galactose intake, patients with intolerance to this sugar receive a high carbohydrate intake to minimize the effects of any galactose inadvertently included in the diet.

FROM THE AUTHORS' SUMMARY.

THE NUTRITIVE QUALITY AND THE TRYPSIN INHIBITOR CONTENT OF SOYBEAN FLOUR HEATED AT VARIOUS TEMPERATURES. R. J. WESTFALL and S. M. HAUGE, J. Nutrition **35**:379 (March) 1948.

A method for determining the potency of the trypsin inhibitor of raw or heated soybean flours is presented by Westfall and Hauge. The protein efficiency increased in direct proportion to the destruction of the potency of its trypsin inhibitor by heat. Since the trypsin inhibitor is the cause of the poor utilization of raw soybean protein, the minimal heating conditions for destroying the inhibitor should yield a soybean flour of optimal quality.

FREDEEN, Kansas City, Mo.

THE EFFECT OF INANITION ON MAMMARY-GLAND DEVELOPMENT AND LACTATION. J. F. SYKES, T. R. WRENN and S. R. HALL, J. Nutrition **35**:467 (April) 1948.

Inanition in rats from weaning through pregnancy reduces growth of the mammary gland to a greater extent than might be expected from the reduction in body size which results from reduced feed intake. Sykes and his co-workers observed that when adequate feed was supplied during lactation to rats that had been on the restricted diet they increased in body size rapidly, the mammary gland also grew rapidly, and their lactation performance was superior to that of rats which had an adequate feed intake throughout the whole of the experimental period.

FREDEEN, Kansas City, Mo.

COMPARATIVE GROWTH-PROMOTING VALUES OF THE PROTEINS OF CEREAL GRAINS. D. BREESE JONES, ALVIN CALDWELL and KATHERINE D. WIDNESS, J. Nutrition **35**:639 (June) 1948.

The order of values of some of the grains as compared with each other varied somewhat with the different protein levels at which they were incorporated in the diets. Oats, rice and rye, however, at each of the protein levels at which they were used, proved superior to all the other grains. The growth-promoting values of the proteins of whole yellow corn, hard and soft wheat, pearled barley, brown and polished rice, rye and rolled oats were compared by means of *ad libitum* feeding experiments with young albino rats. As far as their nitrogen contents permitted, the materials were incorporated at 4.5, 7.5, 9.5 and 12 per cent protein levels in diets approximately isocaloric and nutritionally adequate with respect to dietary factors other than protein. The results were evaluated on the basis of increases in weight and gains per gram of protein consumed over six week periods.

FREDEEN, Kansas City, Mo.

THE NUTRITIVE VALUE OF CEREAL PROTEINS IN HUMAN SUBJECTS. CARL A. KUETHER and VICTOR C. MYERS, J. Nutrition **35**:651 (June) 1948.

Rolled oats and exploded oat cereal, as sources of nitrogen, are equally well utilized by adult human subjects when they furnish 55, 80 or 100 per cent of the total dietary nitrogen, the remainder of the nitrogen being furnished by milk, and when the total protein (nitrogen $\times$ 6.25) intake is approximately 0.70 Gm. and the caloric intake approximately 37.5 calories per kilogram of body weight per day. Both cereals furnish suboptimal amounts of lysine. Both wheat flakes and exploded wheat are inferior to unprocessed whole wheat in the maintenance of nitrogen equilibrium. Of the unprocessed cereals in these experiments, the best balance was observed on whole wheat, rolled oats and corn, in that order.

FREDEEN, Kansas City, Mo.

TRENDS IN INFANT FEEDING. MILTON J. E. SENN, Wisconsin M. J. **47**:195 (Feb.) 1948.

One of the trends in infant feeding is the renewal of interest in breast feeding, particularly for its psychologic benefit in establishing good relationships between mother and child. Another trend is toward less coercive and rigid feeding technics. This is in opposition to previous cultural and scientific influences and leaves the pediatrician in the predicament of having to evaluate for himself the various methods and of having to apply them with due regard for his patients as individual persons. "Streamlining" of infant feeding is condemned when it by-passes natural

growth. A third trend, based on chemical and metabolic studies, is the stress on the significance of protein. Especial emphasis is given to the use of formulas high in protein for premature infants, the use of protein enterally and parenterally in disease and the employment of amino acid preparations.

BAIRD, Wauwatosa, Wis.

SELF DEMAND FEEDING IN INFANTS. C. K. ROWAN-LEGG, Canadian M. A. J. **66**:388 (April) 1949.

This is a discussion of the rational idea of self-demand feeding schedules. No new contributions are made.

McGUIGAN, Evanston, Ill.

MILK: A EUROPEAN CHILD HEALTH PROBLEM. HENRY F. HELMHOLZ, Arch. Dis. Childhood **23**:154 (Sept.) 1948.

If by large scale production, the price differential between powdered milk and pasteurized bottled milk can be wiped out in Europe or powdered milk rendered even cheaper, as in the United States at present, powdered milk should prove to be the ideal supply of cow's milk for the infants and children of Europe.

The milk used locally in production areas or in communities without facilities for pasteurization should be boiled before using. All commercial fluid milk should be pasteurized, bottled and refrigerated until used. The use of dried skimmed milk deserves greater attention from the pediatrician for its value as a cheap protein food for children.

KELLY, Milwaukee.

OBSERVATIONS ON THE METABOLISM OF POTASSIUM FROM A STUDY OF THE RENAL CLEARANCE. H. ELLIS C. WILSON, Arch. Dis. Childhood **23**:182 (Sept.) 1948.

Observations on children with and without the administration of potassium citrate by mouth showed that the potassium clearances tend to vary inversely with the plasma level.

In the adult the curve for plasma potassium after the administration of potassium phosphate and citrate, but not after the chloride, falls, while the clearance rises. The conclusion is drawn that the main factor controlling the excretion of potassium is the saturation of the cells with this electrolyte.

There is evidence to show that potassium enters the cells more readily when given as the phosphate or citrate than as the chloride. The significance of this observation in relation to the composition of fluids for intravenous use in combating extracellular and intracellular dehydration is discussed.

KELLY, Milwaukee.

Vitamins; Avitaminoses

THE RELATIONSHIP BETWEEN ASCORBIC ACID AND PHAGOCYTIC ACTIVITY. W. J. NUNGESTER and ADA MAY AMES, J. Infect. Dis. **83**:50 (July-Aug.) 1948.

These studies demonstrate a relationship between the ascorbic acid content of exudative polymorphonuclear leukocytes from guinea pigs and the fragility and the phagocytic activity of these cells. A parallel is also drawn between the level of vitamin C metabolism of the donor animals and the quantity and quality of the exudate obtained from the injection of an irritating substance into their peritoneal cavities.

Serum in the system not only promotes phagocytic activity but also tends to protect the cells from rupture. The amount necessary to afford such protection varies inversely with the vitamin C content of the cells.

FROM THE AUTHORS' SUMMARY.

A STUDY OF THE FASTING-HOUR EXCRETION OF THIAMINE IN THE URINE OF NORMAL SUBJECTS. EVANGELINE PAPAGEORGE and GEORGE T. LEWIS, J. Nutrition **34**:301 (Sept.) 1947.

Assuming that the twenty-four hour excretion of thiamine was a fair index of nutritional status with respect to this vitamin, Papageorge and Lewis concluded that the fasting-hour excretion test could be employed in assessing thiamine status when a large number of persons were to be tested. The critical level of fasting-hour excretion of thiamine appears to be 4 micrograms. Values below this suggest a likelihood of inadequate thiamine intake.

FREDEEN, Kansas City, Mo.

CONGENITAL MALFORMATIONS INDUCED IN RATS BY MATERNAL VITAMIN A DEFICIENCY: II. EFFECT OF VARYING THE PREPARATORY DIET UPON THE YIELD OF ABNORMAL YOUNG. JOSEF WARKANY and CAROLYN B. ROTH, J. Nutrition **35**:1 (Jan.) 1948.

Congenital abnormalities can be induced in the offspring of female rats reared and bred on diets deficient in vitamin A. The abnormalities are seen in soft tissues and are different from those induced in the skeleton by maternal riboflavin deficiency. Warkany and Roth observed that variations of the preparatory diet influence the yield of abnormal young. Increase of the carotene supplement results in an increased fertility rate, but the percentage of abnormal young decreases. Reduction of the carotene supplements reduces fertility, while the percentage of abnormal young increases.

FREDEEN, Kansas City, Mo.

HUMAN UTILIZATION OF ASCORBIC ACID FROM MUSTARD GREENS. MARTHA E. HOLLINGER, J. Nutrition **35**:73 (Jan.) 1948.

Hollinger concluded that some persons utilize the ascorbic acid from cooked mustard greens just as well as the synthetic vitamin preparation.

FREDEEN, Kansas City, Mo.

THE EFFECT OF DIETARY RESTRICTION OF B-COMPLEX VITAMINS AND PROTEIN ON THE EXCRETION OF CREATININE BY HUMAN SUBJECTS. THEODORE E. FRIEDEMANN, VELMA M. KINNEY, GEORGE H. BERRYMAN, CHARLES R. HENDERSON and JOHN B. YOUMANS, J. Nutrition **35**:117 (Jan.) 1948.

Friedemann and his associates concluded that dietary restrictions with respect to protein and vitamin of the B complex resulting in the development of symptoms of deficiency may be reflected in metabolic changes associated with the formation and excretion of creatinine. These changes may persist and are not rapidly abolished during subsequent supplementation.

FREDEEN, Kansas City, Mo.

PRODUCTION OF FUNCTIONAL AND FATTY CHANGES IN THE LIVER BY A CHRONIC VITAMIN B COMPLEX DEFICIENCY, AND INTERRELATIONSHIPS WITH PROTEIN INTAKE. VICTOR A. DRILL and TED A. LOOMIS, J. Nutrition **35**:333 (March) 1948.

In this investigation it was observed that a chronic deficiency of the vitamin B complex in dogs may produce functional and histologic hepatic changes, depending on the protein intake. Drill and Loomis stated that a subnormal amount of the

vitamin B complex can produce functional changes when a normal (20 per cent) casein diet is fed but cannot do so when there is a high protein intake (41 per cent casein). That such hepatic dysfunction in dogs on the 20 per cent casein diet is not due to inanition can be seen by the lack of changes in the inanition-control dogs which received a normal amount of yeast. The fact that such changes did not develop with the high protein diet is evidence indicating some interrelationship of action, in which either the vitamin B complex or the protein level of the diet is the deciding factor. Biopsy specimens of liver showed the presence of large fat droplets, but no necrosis. Inanition controls showed neither functional nor histologic changes. The chronically deficient animals were treated with yeast extract, which restored the hepatic function to normal and produced a disappearance of the large fat droplets in the liver, even though the protein and caloric intakes were restricted during the period of therapy.

FREDEEN, Kansas City, Mo.

THE RELATION OF THIAMINE CLEARANCE TO BLOOD LEVELS IN MAN. M. C. BLANCHAER and EILEEN CAMERON, J. Nutrition **35**:391 (March) 1948.

Blanchaer and Cameron made simultaneous estimations of blood thiamine and thiamine clearance on 23 patients in the hospital. They observed a definite association of low clearance values with poor general conditions. The correlation of lowered thiamine excretion with increased age was considered to be a reflection of the general debility of elderly patients.

FREDEEN, Kansas City, Mo.

THE VITAMIN A CONTENT OF HUMAN BLOOD PLASMA AS AN INDEX OF CAROTENE UTILIZATION. EVA HARTZLER, J. Nutrition **36**:381 (Sept.) 1948.

Hartzler conducted her experiment with a single subject given a diet low in vitamin A for three periods of 166, 80 and 115 days, respectively. Between these three periods were two periods of moderate vitamin A intake of 73 and 163 days, respectively. Her results showed that the plasma level of vitamin A can be used as a measure of the utilization of carotenoids by human beings. The data obtained do not indicate that the blood plasma level is more sensitive than the dark adaptation time as an index of vitamin A nutrition, although the plasma level is undoubtedly a more specific measure.

FREDEEN, Kansas City, Mo.

STUDIES ON BERIBERI IN AN ENDEMIC SUB-TROPICAL AREA. JUAN SALCEDO JR., EUFRONIO O. CARRASCO, FRANCISCO R. JOSE and RAMON C. VALENZUELA, J. Nutrition **36**:561 (Nov.) 1948.

Salcedo and his co-workers made a clinical survey of beriberi in the province of Bataan, Philippines, a subtropical area with the endemic disease. The population surveyed consisted of 11 to 64 per cent of the total population in each of nine of the twelve municipalities of the province. A total of 12,384 persons were examined, and 1,580 persons with frank or suspected beriberi were observed, corresponding to 12.7 per cent of the population. Frank beriberi occurred in 1.99 per cent. Beriberi was seen in descending order of frequency in "expectant mothers," "nursing mothers," "other adults," "infants" and "children." The reported mortality from beriberi was highest in "infants" and then in "other adults," there being no deaths of "expectant mothers" and only a small number among "nursing mothers." Discussion is presented of the frequency of signs and symptoms of clinical beriberi, of the limited usefulness of the so-called fasting hour test for urinary excretion of thiamine, and of the dietary practices of rice eaters in Bataan. The authors see no correlation between the excretion of urinary thiamine in the "fasting hour"

and the severity of beriberi. They are of the opinion that the dietary history and the results of physical examination and the "fasting hour" urinary examination for thiamine should be taken together to form a basis for the diagnosis of beriberi in individual persons and for the assessment of the incidence of beriberi in a community.

FREDEEN, Kansas City, Mo.

INFLUENCE OF THE CONCENTRATION OF MIXTURES OF VARIOUS COMPONENTS OF THE VITAMIN B COMPLEX ON BIOLOGICAL VALUE OF CASEIN AND ON ECONOMY OF FOOD UTILIZATION. BARNETT SURE and FREELAND ROMANS, J. Nutrition **36**:727 (Dec.) 1948.

Sure and Romans state that the purpose of their study was to investigate the influence of the concentration of synthetic mixtures of the vitamin B complex on protein efficiency and on economy of total food utilization. An increase in the concentrations of thiamine, riboflavin, pyridoxine, nicotinic acid, pantothenic acid, choline, paraaminobenzoic acid and inositol used in synthetic mixtures as sources of the vitamin B complex resulted in decided increases in growth and food utilization. Increases in nitrogen retention and protein synthesis occurred only within a narrow range of the low concentration of the vitamin B complex. The pronounced increases in growth were due largely to fat synthesis from the carbohydrate (cerelose) in the rations. On a low 7.1 per cent protein level some growth was possible, but only when the various components of the vitamin B complex were raised to high concentrations. On the same low protein intake and on a low concentration of the B vitamins, only maintenance was obtained during a one week experimental period. The results of feeding aqueous butyl alcohol extracts of 1:20 Wilson's concentrate powder as a source of unknown components of the vitamin B complex were negative, as far as utilization of casein for growth was concerned.

FREDEEN, Kansas City, Mo.

THE ABSORPTION OF OILY AND AQUEOUS PREPARATIONS OF ESTER AND ALCOHOL VITAMIN A BY NORMAL CHILDREN AND CHILDREN WITH VARIOUS DISEASES. AUGUSTA B. MCCOORD, CHRIS P. KATSAMPES, C. FRED LAVENDER, FREDERICK J. MARTIN, R. A. ULSTROM, R. H. TULLY III and ALICE J. KEENAN, Pediatrics **2**:652 (Dec.) 1948.

Absorption of oily preparations of ester and alcohol or "predigested" vitamin A (210,000 international units per gram) by 32 newborn infants, 13 older children and 12 adults was compared. These normal subjects were given 7,000 international units per kilogram of body weight of vitamin A orally. Blood specimens taken four and seven hours later showed that the maximum concentration occurred at about four hours. After ingestion of ester vitamin A, mean concentrations for newborn infants, older children and adults were, respectively: 502, 1,569 and 1,300 international units of vitamin A per hundred cubic centimeters of serum. After ingestion of alcohol vitamin A, corresponding values were 688, 817, and 1,273 international units.

Thirteen children with cystic fibrosis of the pancreas absorbed alcohol vitamin A much better than the ester, while 7 children with celiac disease absorbed both poorly, thus providing an aid in the differential diagnosis. Patients with giardiasis, diarrhea, anemia and severe malnutrition absorbed alcohol vitamin A in oil much better than the ester.

Absorption of aqueous and oily preparations of ester and alcohol vitamin A was also compared. The test dose was 14,000 international units per kilogram of body weight of vitamin A. The concentration in serum was determined three, four, five and six hours after ingestion. We did not observe such a striking difference in

absorption of aqueous and oily preparations as have other investigators, possibly because of the kinds of oily preparations used.

Maximum serum concentration occurred three to four hours after ingestion of aqueous preparations and four to five hours after that of oily ones. In most cases, administration of aqueous preparations produced somewhat higher concentrations. Vitamin A in serum remained elevated longer after ingestion of oily preparations. Patients with celiac disease, intestinal ulcers and other diseases absorbed both poorly; others exhibited excellent absorption of both.

FROM THE AUTHORS' SUMMARY.

SKELETAL CHANGES IN GROWING VITAMIN B COMPLEX DEPLETED RATS AND THE COURSE OF REPAIR. MARTIN SILBERBERG, BARNET M. LEVY and FRED YOUNGER, Proc. Soc. Exper. Biol. & Med. **67**:185 (Feb.) 1948.

Thirty-five rats, 19 to 22 days old, were kept in three groups: (1) those given a stock diet, (2) those given a vitamin B-free diet and (3) those given a deficient diet then refed the stock diet. The upper end of the tibia and lower end of the femur were removed about three weeks after the feeding. Slides stained with hematoxylin and eosin were prepared for histologic studies. The width of the epiphysial disk and of the cortex of the tibia was measured, as well as the number of traberculae in the metaphysis of the tibia in a given area. It was observed that in the growing rat on a diet deficient in vitamin B complex there was retardation and, finally, cessation of growth of cartilage and bone, associated with serous atrophy of the bone marrow. The male animals were more sensitive to the deficiency than the females. After the refeeding of a stock diet, skeletal growth was resumed at an intensified rate.

HANSEN, Galveston, Texas.

Hygiene; Growth and Nutrition; Public Health

FOLLOW-UP OF MEDICAL RECOMMENDATIONS. MARTHA CRUMPTON HARDY, J. A. M. A. **136**:20 (Jan. 3) 1948.

An extensive survey was made on 1,068 Chicago "well" children representing 446 families selected from all over the city who were not registered at any clinic or agency. These children were examined by the pediatric staff of the Elizabeth McCormick Memorial Fund between September 1942 and August 1943, and various medical and dental recommendations were made. A few families had private physicians, but most of them had to depend on clinics for their care. Of the 446 families, only 5 families needed no care. In addition, 113 families moved or were lost before the survey was complete.

Of the remaining 789 children, representing 328 families, for whom medical and dental care was recommended, 35 per cent carried out all the recommendations for the family, 31 per cent some of the recommendations, 14 per cent few or none and 20 per cent none.

KIMBALL, Evanston, Ill.

EFFECTS OF NITRATES IN RURAL WATER SUPPLIES ON INFANT HEALTH. JAMES G. WEART, Illinois M. J. **93**:131 (March) 1948.

Infantile methemoglobinemia, with possibly severe cyanosis, may result from the use of feeding formulas incorporating water which contains the nitrate ion in toxic amounts. The Sanitary Engineering Division of the Illinois Department of Public Health found that Illinois well waters containing large amounts of nitrates occur with a frequency never before anticipated.

In various sections and counties of the state, from 20 to 25 per cent of the waters from rural wells were found to contain more than 10 parts per million of nitrate nitrogen. Ten parts per million of nitrate nitrogen is considered the maximum that can safely be used for infant feeding.

A simple colorimetric test for nitrates can be used to determine quickly the approximate nitrate content of water. Emergency treatment of acute cases of cyanosis resulting from methemoglobinemia consists of the intravenous injection of 1 per cent solution of methylene blue.

No correlation can be discovered between the nitrate content of these waters and the sanitary quality. No satisfactory explanation has been found for the occurrence of these large amounts of nitrate. There is neither a practical treatment that will remove the nitrates from the water nor any method of well construction that will obtain better water. Three cases are reported.

BARBOUR, Peoria, Ill.

SPEECH SURVEY METHODS IN PUBLIC SCHOOLS. VANETTA R. SUYDAM, J. Speech & Hearing Disorders **13**:51 (March) 1948.

Four principal methods for locating children in need of speech training are now used by speech clinicians: The first is the referral method in which classroom teachers, principals, parents and others refer to the correctionist children needing remedial work in speech; the second is the speech survey; the third is a combination of referral and survey, and the fourth is voluntary enrolment by patients. The speech survey generally consists of (1) a questionnaire, (2) a personal interview or (3) a combination of questionnaire and personal interview. A study of survey methods used in this country shows that a child needs to be surveyed only once. Teachers should notify correctionists of those children who need retesting. If each child is given a "sweep" test following which those with doubtful ratings are retested, the results are more reliable. Methods used in speech surveys should be adapted to the needs of the individual clinician, the children tested, the community and the situation. Speech surveys are an essential part of a clinician's work.

PALMER, Wichita, Kan.

GUIDANCE IN MATERNAL AND INFANT CARE TWO MONTHS BEFORE AND AFTER THE BIRTH OF THE FIRST-BORN. AUGUSTA STUART CLAY, Pediatrics **2**:200 (Aug.) 1948.

To discover the type of guidance parents want, the type offered and the type needed, 11 couples were visited weekly; 10 mothers were from clinics of the New Haven Hospital, New Haven, Conn., and 1 was a patient of a private physician. Records showed no problems save those of healthy pregnancy.

Most parents did not want classes but preferred to discuss personal problems, their childhood and the care of mother and baby with a consultant in their home. Those with a happy childhood expected to enjoy the baby; those less fortunate, to discipline and train.

When medical care was explained, parents became more cooperative and competent. When they learned that the mother's sudden hunger, fatigue and cramps resulted from her rapid growth in pregnancy and that the baby would feel the same way after birth, they realized that he would be irritated by imposed routines. Desire for knowledge followed a definite sequence. The more parents learned about the way in which the baby developed before and after birth, the more they realized he was a person, not a possession.

Many wanted to be together during labor and delivery and when the mother nursed. The mother wanted to be taught how to nurse. Five couples wanted the

baby in the mother's room. One had this privilege. Only the husband and mother visited. The baby nursed when hungry. On going home, they had no confusion or diminishing of breast milk as the others had experienced.

The five mothers who breast fed the babies four months or longer took best care of themselves and the babies. Their babies were healthiest and happiest. Parents said the discussions helped them understand how mother and baby developed and how to meet their needs. They felt freer to talk together with a consultant than with different doctors who were busy or uninterested in personal problems. They were confused by conflicting guidance from obstetricians, pediatricians and nurses. They gave the consultant information withheld from doctor, nurse and social worker but pertinent to diagnosis.

From the Author's Summary.

Acute Contagious Diseases

Poliomyelitis: Study of an Epidemic of Forty Cases in Key West, Florida, May-August 1946. W. Dalton Davis and Charles M. Silverstein, Arch. Neurol. & Psychiat. **58**:740 (Dec.) 1947.

The authors studied 40 verified cases of poliomyelitis and 190 cases of suspected or abortive attacks on the islands of Key West. Of the patients, 73.7 per cent were adults in the United States Navy (19 to 33 years of age) and 10.5 per cent were adult civilians. There were 3 instances in which 2 verified cases occurred in the same family. Eight patients had a normal temperature when admitted to the hospital. A history of direct contact with persons known to have poliomyelitis was obtained for 18 (almost one half) of the patients.

Beverly, Oak Park, Ill.

Recent Advances in the Diagnosis and Prevention of Mumps and Measles. Harold E. Pearson, California Med. **67**:230 (Oct.) 1947.

Recent experimental work offers good prospects of the development of diagnostic cutaneous tests and immunizing agents against mumps, measles and rubella.

Pryor, Redwood City, Calif.

Field Studies in Bacillary Dysentery in U. S. Military Personnel and Civilians in North Africa and Italy: II. Pathogenicity of a New Serologic Type of Dysentery Bacillus (T-2nd Med. Lab. or Lavington I or Etousa). A. H. Stock, W. W. Tribby and A. Ashute, J. Infect. Dis. **81**:65 (July-Aug.) 1947.

An epidemic in United States troops in Casablanca due to a new serologic type of mannite-fermenting dysentery bacillus (type T-2d Med. Lab., Lavington I or etousa) is described. The explosive onset of the infection and the pattern of spread suggested transmission by infected food handlers and person to person contact. Type T strains were also recovered from United States troops in Italy.

Toomey, Cleveland.

Field Studies in Bacillary Dysentery in U. S. Military Personnel and Civilians in North Africa and Italy: III. The Epidemic of Bacillary Dysentery in the Atlantic Base Section, French Morocco, 1943. A. H. Stock, A. G. Karlson, W. W. Tribby and J. H. Hill, J. Infect. Dis. **81**:68 (July-Aug.) 1947.

Data are presented to show the widespread distribution of the epidemic of bacillary dysentery in the United States troops stationed in French Morocco in 1943. Person to person contact was probably significant and food handlers were likely vectors.

Toomey, Cleveland.

CAN DROSOPHILA FLIES CARRY POLIOMYELITIS VIRUS? JOHN A. TOOMEY, P. P. PIRONE, WILLIAM S. TAKACS and MORRIS SCHAEFFER, J. Infect. Dis. **81**:135 (Sept.-Oct.) 1947.

Fresh virulent virus (Lansing strain carried in mice) does not seem to multiply in a strain of fruit flies (Drosophila melanogaster). The insect can be grossly contaminated to the point where it retains sufficient virus to cause paralysis in a few experimental animals. These flies, like the common housefly (Musca domestica), do not appear to be of epidemiologic importance in poliomyelitis, since the authors were unable to transfer the virus from flies exposed to it, except under conditions probably not present in nature.

TOOMEY, Cleveland.

THE TREATMENT OF THE MUSCULAR AFTER-EFFECTS OF POLIOMYELITIS. MILAND E. KNAPP, Minnesota Med. **30**:1152 (Nov.) 1947.

The author states that the after-effects of poliomyelitis cannot be removed by medication, and at present no effective methods are known for preventing them. Therefore, their treatment resolves itself into the solution of various mechanical problems. These are explained in the paper, and the statement is made that the carrying out of motion in the nearest possible approach to the normal manner is the most important part of treatment and that the development of maximal strength in order to have smooth, rhythmic function in as normal a manner as possible may be sacrificed. Artificial support and braces are to be avoided so far as possible. It may be necessary to use some form of support in order to prevent an excessive backknee or rotation of the foot in such a manner that walking is impossible.

STOESSER, Minneapolis.

VASOMOTOR DISTURBANCES IN POLIOMYELITIS, WITH SPECIAL REFERENCE TO TREATMENT WITH PARAVERTEBRAL SYMPATHETIC BLOCK. VINCENT J. COLLINS, WILLIAM L. FOSTER and WILIAM J. WEST, New England J. Med. **236**:694 (May 8) 1947.

Vasomotor disturbances, such as edema, hyperhidrosis, coldness and chilblains, are frequently encountered in the convalescent period of poliomyelitis. Sympathetic nerve blocks were employed to alleviate these distressing manifestations of disturbed vasomotor activity, with partial to complete relief in 15 of the 17 patients treated. Pain, muscle spasm and muscle tenderness were completely relieved in 3 patients by sympathetic nerve blocks and without supplementary therapeutic measures, such as physical therapy and use of hot packs.

It is suggested that the pain, tenderness and muscle spasm in the acute phase of poliomyelitis may also be alleviated by sympathetic nerve blocks. It is questionable whether this treatment would be applicable to children unless general anesthesia could be used.

GENGENBACH, Denver.

ECZEMA VACCINATUM. A. DANIEL RUBENSTEIN, New England J. Med. **237**:395 (Sept. 11) 1947.

A case of eczema vaccinatum is presented in which the infection occurred as a result of contact with a vaccinated sibling. The clinical diagnosis was confirmed by a positive reaction to the Paul test.

Precautionary measures, such as deferring vaccination of patients with cutaneous disorders and preventing exposure of such patients to vaccinated persons, will reduce to an even greater extent the present low incidence of generalized vaccinia, a ratio of 1 case in 20,000 to 40,000 vaccinations. A case fatality rate of 33 per cent has been reported for eczema vaccinatum.

GENGENBACH, Denver.

DIRECT ISOLATION OF MUMPS VIRUS IN CHICK EMBRYOS. GLEN R. LEYMASTER and THOMAS G. WARD, Proc. Soc. Exper. Biol. & Med. **65**:346 (June) 1947.

Saliva was collected during the acute inflammatory stage from 9 patients with mumps, the material emulsified, centrifuged with additions of penicillin and streptomycin, then inoculated into the amniotic sac of eight day chick embryos. Usually about 10 eggs were injected and allowed to incubate for seven days at 35 to 36 C. (95 to 96.8 F.). They were tested for virus with washed chicken erythrocytes, and fluids which gave a positive hemagglutination reaction were repassed amniotically. The infectious agent was identified as mumps virus by a complement fixation reaction with acute and convalescent human mumps serum. Two samples were also studied by injection into the parotid glands of monkeys. Mumps virus was isolated from 8 of the 9 patients with clinical mumps.

HANSEN, Galveston, Texas.

POLIOMYELITIS PREPAREDNESS. GEORGE D. WILSON, South. M. J. **40**:899 (Nov.) 1947.

A discussion is given of the teamwork necessary among the various medical specialists, nurses, public health officials, vocational rehabilitation directors, brace makers and physical therapists so that any state may be prepared for a poliomyelitis epidemic. The roles of the National Foundation for Infantile Paralysis, and federal and state agencies are also cited.

LOGAN, Rochester, Minn.

EARLY TREATMENT OF POLIOMYELITIS BY MEANS OF METHENAMINE IODOBENZOMETHYLATE AND SODIUM SALICYLATE. J. H. CHARBONNEAU, Union méd. du Canada **75**:663 (June) 1946.

The author has been using sodium salicylate and the iodobenzomethylate of hexamethylenetetramine in the treatment of the acute stage of poliomyelitis. These two drugs pass into the spinal fluid and appear to act directly on neurotropic viruses. Histories of 11 cases are presented in which the treatment produced amazingly good results. The drugs were administered intramuscularly or intravenously. The dosage varied considerably, but in the author's opinion 0.1 to 0.16 Gm. of each per kilogram of body weight per day represents the optimum dosage. In many cases injections of calcium gluconate were given empirically.

DEFFINEE, Melrose, Mass.

HARMFUL EFFECTS OF VACCINATION AGAINST SMALLPOX IN THE CANTON OF BERN SINCE 1941. FELIX OESCH, Ann. pædiat. **169**:125 (Aug.) 1947.

Postvaccination encephalitis has occurred in the canton of Bern since 1944 and in other parts of Switzerland as well. Approximately 2 in 10,000 of all persons vaccinated for the first time were affected. The age of the affected children was never under 16 months. The incubation period in all persons was between five and fifteen days, as ascertained earlier by Glanzmann, with one exception (twenty days in case 3).

As no details are known concerning the pathogenesis, prophylaxis against this most dreaded complication can be achieved only by careful anamnesis and selection, as well as by persistent vaccination of infants before the sixteenth month, as prescribed by the Federal Health Ministry.

FROM THE AUTHOR'S SUMMARY.

INFLUENCE OF THE WAR ON INFANTS' DYSENTERY IN BUDAPEST. T. BAKÁCS, Ann. pædiat. **169**:136 (Aug.) 1947.

Morbidity and mortality due to dysentery exhibited an increase in 1945 which was mainly due to the involvement of the metropolis in the events of the war. After the war, as the eliciting cause ceased, rehabilitation did not occur soon enough, especially in regard to the development of the children in the youngest age group. For this reason, the epidemics in 1945 were grave. In connection with the epidemics the differences existing among the districts of the city from the point of view of social, economic and hygienic conditions and their influence on mortality are pointed out.

The extent of rehabilitation is evident from the fact that today there are 26 institutes for the protection of mothers and children as against 20 such institutes in prewar time, in addition to the great increase in the number of patients. Collection of mother's milk was so organized that every newborn infant not fed by the mother or fed unsatisfactorily receives, according to his needs, a proper complement. A network of milk kitchens capable of providing all the children requiring milk is being erected.

The Nazi regimen not only took its victims in the field but caused much destruction in the hinterland even after the war among those possessing the minimum of resistance, whose lives were highly important for the future, that is, among the newborn infants and children. In the course of return to normal, the liberation of young children from this imminent danger seemed the first duty. Apparently, for the major part, this has been done, as may be seen from the infant mortality rate for 1947, which is lower than that for the best years of peacetime. The final goal, beyond the results obtained so far, is to surpass the prewar conditions, chiefly by eliminating the social differences still partially existing and by increasing the standard of living of the most backward classes. These are the guiding principles of the present and the future, and it is hoped that they will be attained.

FROM THE AUTHOR'S SUMMARY.

SEPSIS FROM SCARLET FEVER OTITIS IN A BOY, THREE YEARS OLD, WITH PENICILLIN. VÁCLAV KREBA, Pediat. listy **2**:249, 1947.

A case of scarlet fever is described in which sepsis developed from bilateral mastoiditis. As a result of treatment with penicillin, the general and local signs of mastoiditis were suppressed. Thus, loci developed which led to generalized sepsis, with endocarditis, myocarditis, nephritis and bronchopneumonia. Besides the usual nephritic edema, a peculiar elastic edema formed, which was painful to touch. This was localized on the neck and the chest and filled the supraclavicular and infraclavicular spaces. After a one-sided antrotomy, only slight improvement was observed, whereas after trepanation on the other side, cure followed quickly.

FROM THE AUTHOR'S SUMMARY.

PENICILLIN THERAPY IN BRONCHOPULMONARY COMPLICATIONS OF WHOOPING COUGH. A. MASI and M. GIUSTI, Rev. clin. pediat. **45**:332, 1947.

The authors, after reviewing the most frequent respiratory complications during whooping cough, with special regard to bronchopneumonia, describe the most characteristic anatomopathologic, roentgenologic and clinical aspects of this complication.

The therapeutic results obtained in 30 cases of bronchopneumonia associated with whooping cough, treated with penicillin, are reported.

FROM THE AUTHORS' SUMMARY.

FAMILIAL POLIOMYELITIS: REPORT OF CASES. RAUL MAGGI, Rev. Asoc. méd. argent. **59**:302 (April 15) 1945.

Thirty-six of 600 cases (6 per cent) of poliomyelitis observed during the epidemic of 1942-1943 were familial, more than 1 case occurring in 17 families. In 15 families there were 2 cases each; in 2 families there were 3 cases each. In 8 instances the second case appeared simultaneously with the first; in 9 cases the second case came on from the third to the seventeenth day after the initial case in the family. In 2 cases no data were available on the interval between the primary and the secondary cases. Twenty-eight cases were of the paralytic and 8 of the nonparalytic forms. Paralytic phenomena were more frequent in the initial cases.

SAVITSKY, New York [ARCH. NEUROL. & PSYCHIAT.].

ENDEMIOLOGIC DATA AND SPECIAL ASPECTS OF AN OUTBREAK OF POLIOMYELITIS IN CUBA. J. F. BACARDI and F. R. CORRIA, Rev. Cubana de pediat. **19**:539 (Dec.) 1946.

Three hundred and forty-three cases of poliomyelitis were reported in Cuba in 1946. The largest number appeared early, in April and May, and the incidence fell abruptly in the hottest months, July and August.

It appeared that some factor not yet known was responsible for simultaneous infection in separate communities. In two different communities it was suggested that the water supply might be the source of infection, although the virus was not shown to be present. In one community the cases were limited to an area supplied from one source of water. In another, an island, the water supply was found to be contaminated with other organisms.

KEITH, Rochester, Minn.

PULSE RATE AND TEMPERATURE IN DIPHTHERIA. P. BAMBERGER, Arch. f. Kinderh. **133**:191 (April) 1947.

For this study only cases of typical faucial diphtheria were selected; cases of laryngeal diphtheria were excluded because of the complications caused by mechanical obstruction. The case histories of 1,301 patients who recovered were compared with those of 317 patients who died. The body temperature was found to be high in diphtheria, as in all other severe infectious diseases. Contrary to the statements in most textbooks, the temperature, as a rule, was found to be higher the severer the diphtheritic infection was. Without therapy the temperature remained high for the first four days. After suitable doses of antitoxin, the patient's temperature became normal or nearly normal within a few days when the prognosis was favorable. When the course of the diphtheria was unfavorable, the temperature dropped much more slowly. Subnormal temperature, an especially ominous sign, was not observed before the end of the first week or early in the second week of the disease.

The pulse rate in diphtheria is higher, as a rule, than would correspond to the temperature readings. This discrepancy is more pronounced in cases with unfavorable prognosis. Even after suitable doses of antitoxin, the pulse rate does not return to normal during the first eight days of the disease.

ARON, Chicago.

OBSERVATIONS ON TYPHUS AMONG CHILDREN. H. W. OCKLITZ, Ztschr. f. Kinderh. **65**:18, 1947.

During the winter of 1945-1946, 79 children with exanthematous typhus (58 proved cases in children with fever on their admission to the hospital) were seen by the author. The importance of the hygienic conditions is borne out by

the fact that only 6 were not refugee children. No patient was under 2 years of age. The disease presented itself in a noncharacteristic influenza-like picture, with fever, headache, abdominal pain, sore throat, sleepiness, thirst and slight cough. Body weight was usually below normal, but fat children seemed to show a severer picture of illness, as also observed in scarlet fever and diphtheria. The average duration of fever was ten to thirteen days. Twenty-six of the 58 patients with fever had no cutaneous lesions. The face appeared swollen like that of a drunkard. Many children showed conjunctivitis; the cheeks had a strange, pastel, rose-violet sheen. The exanthem usually appeared on the fourth to fifth day, located on the trunk and consisting of rose-brown maculas of pinhead to lentil size. Excision of the roseolar eruption was done in 20 children, and the material was diagnosed as typical for typhus in 15 of them by microscopic examination. There was occasional scaling.

The cardiocirculatory and central nervous systems were most affected. Temporary myocardial damage was diagnosed by auscultation and fluoroscopy. The pulse rate usually corresponded to the temperature. Only one third of the patients showed the typical early bradycardia with subsequent tachycardia. Thirty-nine of the 58 patients had signs referable to the central nervous system. Severe frontal headache was the most frequent symptom, with only little relief on administration of aminopyrine (pyramidon®) and lumbar puncture. Emotional changes occurred frequently: delirium in 3 patients and slowing of speech, excitement, tremors and decreased hearing in others. Reflexes were usually increased. These manifestations disappeared with the return of the temperature to normal. No permanent damage to the central nervous system was seen. The spinal fluid was under increased pressure and showed a positive Pandy reaction. The Weil-Felix reaction of the spinal fluid became positive on the eighth to tenth days. The sugar level was normal or increased early and dropped between the twelfth and fifteenth days to 40 mg. per hundred cubic centimeters, then regained a normal level. The cells observed were usually lymphocytes; red blood cells (20 to 30) and ependymal cells (20 to 40) were seen constantly. These spinal fluid findings were indicative of typhus encephalitis.

Conjunctivitis and conjunctival roseola were noted. Fundoscopic changes were seen in several patients. The tongue was characteristically covered with a furry white to gray-brown coat; the ventral surface was usually of a bluish tinge, the tip and lateral edges free of coating. One third of the children had mild bronchitis. The liver and spleen were palpable in more than one half of the patients.

Albuminuria was noted; one half of the children had white blood cells in the urine; a few showed red blood cells, explained by nephritis and the increased capillary permeability seen in typhus. The sedimentation rate (Westergren) averaged 30 to 60 mm. during the first week. The Weil-Felix reaction of the blood serum became positive (1:200) usually on the sixth to seventh days. One third of the patients showed a positive Widal reaction (1:200 to 1:400), which might in part have been due to previous immunization. Myocarditis occurred in one third of the children, yet it was not a serious complication. Typhoid complicated 9 of the 79 cases and offered differential diagnostic difficulties.

No specific therapeutic agent is effective in the treatment of typhus, but, prophylactically, the improvement of hygienic conditions (removal of body lice) could reduce the incidence because the body louse seems to be the only mode of transmission of this disease.

GLASER, Chicago.

AN EPIDEMIC OF POSTVACCINAL MENINGOMYELOENCEPHALITIS. J. J. KEYZER and P. P. M. NIEUWENHUIS, Maandschr. v. kindergeneesk. **15**:403 (Dec.) 1947.

In the spring of 1947, 27 cases of smallpox were reported in Belgium. In order to prevent the spread of smallpox over Holland, a large part of the population of the southern provinces, Limburg and Brabant, was vaccinated. In Tilburg, Netherlands, 27 patients with postvaccinal encephalitis were hospitalized. All were vaccinated for the first time and became ill after an average incubation period of 11.8 days; the age of the patients varied from 7 to 16 years.

The symptoms were fever, coma, paralysis of the lower limbs, hyperesthesia, spasm of the bladder or incontinence, stiffness of the neck and a positive Kernig sign. The cerebrospinal fluid contained 600 to 700 cells per 3 cu. mm.; the reactions of Nonne and Pandy were positive, and the sugar content varied. Examination of the blood revealed moderate leukocytosis and a slightly accelerated erythrocyte sedimentation rate. Two children died; the others recovered without mental or physical defects. No encephalitis occurred in children between 0 and 6 years of age. The high morbidity of 1.8 per thousand in the children 6 to 11 years old is comparable with that recorded in Switzerland. In 1944-1945, the frequency of encephalitis after first vaccination was reported as 1 to 2 per thousand in the district of Basel; the age of the patients varied between 1½ and 10 years. To explain the high morbidity in Tilburg, Netherlands, it is not necessary to assume the existence of local factors, for the incidence can readily be understood from the age distribution of the vaccinated children. It is concluded that the occurrence of postvaccinal encephalitis can be prevented by vaccinating all children before the end of the first year of life.

VAN CREVÉLD, Amsterdam, Netherlands.

PERTUSSIS ENCEPHALITIS. MARCEL GRAFFAR, Acta pædiat. belg. **1**:97, 1946-1947.

A brief historical review points out the incidence of neurologic complications of whooping cough. The author observed that convulsions became much less frequent during the last years of the study (the incidence was 2.2 per cent from 1938 to 1941). Five case reports with 2 deaths show that the mortality rate also decreased; others report a 50 to 87.5 per cent decrease. One of the reasons for the low mortality rate may be the more advanced age of the patients observed by this author.

The type of convulsions was extremely variable, and some were followed by transitory or permanent paralysis. The pathogenesis of the convulsions was, in the author's opinion, massive cerebral hemorrhages, edema and hyperemia, tetany, gas emboli from ruptured alveoli or inflammatory lesions of the nervous centers. None of these causes seems to stand careful pathologic investigation. Microscopically, the author observed degenerative processes in the cerebral cells. These degenerative processes were attributed either to the direct action of the endotoxin of the Hemophilus pertussis organisms or to vasomotor disturbances. The latter is possible on the basis of reflex angiospasms producing ischemia or toxic disturbances of the wall of the blood vessels.

GLASER, Chicago.

CONTAGIOUS ERUPTIVE FEVER WITH UNUSUAL SYMPTOMS IN INFANCY: REPORT OF TWELVE CASES. S. ZIMANYI, Paediat. danub. **2**:208 (Oct.) 1947.

The benign disease described occurs after an incubation period of five days with alarming symptoms, characteristic petechial eruption and simultaneous high fever, without angina and other catarrhal symptoms. It seems to be contagious and differs essentially from the described contagious diseases with eruption and fever hitherto reported.

It is striking that the disease was observed at the climax of a measles epidemic but that all the symptoms were well distinguishable from those of other well known diseases. Further, although only a few cases occurred, the disease may be considered infectious.

The disease reported is of unknown origin. It is common knowledge that especially in these days after the war there are many infectious and contagious eruptive diseases with a polymorphous course, the differentiation of which is sometimes difficult. Many of them seem benign because complications cannot be observed either immediately or later on. In the literature and the textbooks, most of them are neglected or the data referring to them are contradictory. I believe that more attention to them would result in revealing their practical importance, especially as regards their complications, which are unknown as yet.

FROM THE AUTHOR'S ABSTRACT.

WHO IS MOST IN NEED OF PROTECTION AGAINST MEASLES? GYULA TAMÁSI, Orvesok lapja **2**:1328 (Nov. 1) 1946.

Children who are exposed to infection with measles are divided into two groups in regard to prevention: (*a*) those requiring absolute prevention, which makes an outbreak of measles impossible and which should be used for infants and children up to 3 years of age, children with any other infectious diseases or tuberculosis, without regard to age, and, generally, every child up to 5 years of age with a positive tuberculin reaction, infants and children in hospital wards, pregnant women who have not had measles before and newborn infants of mothers who have measles, and (*b*) those requiring relative prevention, i. e., the development of modified measles, which secures a lifelong immunity and which should be given to healthy children over 3 years of age.

For absolute prevention, infants should receive 10 cc. of convalescent serum or 20 cc. of mixed adult blood. Children between 1 and 3 years should be given 15 cc. of convalescent serum or 30 to 40 cc. of mixed adult blood. These doses should be given during the first half of the period of incubation, whereas in the second half doses should be increased 50 per cent. It is advisable to administer the increased doses even in the first five days of the incubation period to sick infants and children. An amount of blood greater than 40 cc. should not be given, even to older children, on account of technical difficulties.

GÖRGÉNYI-GÖTTCHE, Budapest, Hungary.

Acute Infectious Diseases

NEUROLOGICAL COMPLICATIONS TO TREATMENT WITH RABIES VACCINE. FRANCIS H. REDEWILL JR. and LAURENCE J. UNDERWOOD, California Med. **66**:360 (June) 1947.

A study of 5 cases of neurologic complications on treatment with rabies vaccine seen at the Contagious Disease Unit of the Los Angeles County Hospital is presented, with an analysis of the important clinical findings and their correlation to those cases previously reported.

The incidence of complications in this area is high, but not such that one is warranted to withhold the Pasteur treatment when it is indicated. However, the treatment with vaccine should be given with due regard for the severer reactions. Treatment is best suspended with the occurrence of significant neurologic signs or symptoms.

FROM THE AUTHORS' SUMMARY.

INFLUENZA BACILLUS INFECTIONS AND PENICILLIN. W. HIRSCH and E. NASSAU, Ann. pædiat. **168**:289 (June) 1947.

Three cases of meningitis, 2 cases of empyema and 1 case of osteomyelitis in infancy are described. They were caused by influenza bacilli and the patients were successfully treated with penicillin. These general directives for the treatment of purulent infections caused by penicillin-sensitive strains of influenza bacilli are given: In each case of meningitis, pleural empyema and osteomyelitis in a young child or an infant, one should without hesitation give penicillin intrathecally, intrapleurally or intramuscularly repeatedly until not only the type of organism is known but also whether it is sensitive to penicillin or not. The latter quality alone will decide whether penicillin treatment should be continued. In our cases of empyema and osteomyelitis, treatment with penicillin alone in large enough doses was sufficient. Combined treatment with penicillin and sulfadiazine seems to be the method of choice in meningitis caused by influenza bacilli.

FROM THE AUTHORS' SUMMARY.

TOXOPLASMOSIS IN CHILDHOOD. EDUARD GLANZMANN, Bull. Schweiz. Akad. d. med. Wissensch. **2**:345 (May) 1947.

The protozoan disease of toxoplasmosis is of an anthropozoan type which is transmitted by animals to human beings. There may be completely healthy carriers of Toxoplasma who transmit the pathogenic micro-organisms. Women, during the period of pregnancy, do so by way of the placenta to the fetus. A fetal toxoplasmic encephalitis occurs, connected usually with bilateral chorioretinitis of the macular region. As a rule, the fetal toxoplasmic encephalitis ends fatally in the first weeks of life, but some children survive. The syndrome of hydrocephalus or microcephalus, with intracranial sclerosis, especially of the choroid plexus, and the presence of a unilateral or bilateral microphthalmos, enophthalmos or bilateral macular coloboma are of pathognomonic importance for diagnosis. A certain diagnosis can be secured only by the so-called neutralization test. Bamatter (Geneva) was the first to observe toxoplasmic encephalitis in the newborn in Switzerland.

This report deals with 2 girls, 14 months and 7 years 5 months of age, both with congenital toxoplasmosis. In the first child, the following symptoms were observed: extrapyramidal rigidity of the extremities, idiocy, internal hydrocephalus with intracranial calcifications and bilateral macular coloboma. The symptoms of the second child were gross tremor, stiffness of the legs with talipes equinus, mental debility and, above all, pronounced dwarfism. The roentgenographic findings were calcifications in the three cavities of the skull with osteosclerosis of the skull and extremities, the ends of which were peculiarly goblet shaped. The endochondral bone formation was missing. Microphthalmos and enophthalmos were bilateral. The 2 children showed no significant changes in the values for calcium, phosphorus and phosphatase. In contrast to the situation in toxoplasmic encephalitis of the newborn, the cerebrospinal fluid showed no xanthochromia and no significant augmentation of protein. In the third child, a 4 year old boy, microcephalia, intracranial calcifications and diffuse foci of chorioretinitis were observed.

FROM THE AUTHOR'S SUMMARY.

HEMOGLOBIN METABOLISM IN INFANTILE VISCERAL LEISHMANIASIS DURING ANTIMONY TREATMENT. ANTONIO CROSCA, Arch. ital. pediat. e. puericol. **11**:409, 1946.

In 12 children from 22 months to 7 years of age with infantile visceral leishmaniasis, the author studied the behavior of hemoglobin exchange before, during and at the end of, as well as sometime after, treatment. He concluded that in

infantile visceral leishmaniasis the hemoglobin exchange shows no variation during or at the end of treatment if it was normal before treatment. On the contrary, in the children in whom the hemoglobin exchange was accelerated before treatment, it became normal or had a tendency toward normal at the end of treatment. In only a few children was it increased during or toward the end of the antimony therapy, and in these children it became normal again soon after the end of treatment or within a few weeks. The negative phase of antimony treatment, as observed in several children, often coincided with an acceleration of the hemoglobin exchange; therefore, this increase may have a predominant role in, if it is not the exclusive cause for, the genesis of anemia. In several other children the cause was to be sought exclusively in the disordered hemoglobin exchange that occurs in some instances at the end of, or some time after, the treatment. This malfunction is probably due to a higher degree of blood destruction and more greatly decreased blood formation in the reticuloendothelial system. A persistent increase in the exchange must be considered as a sign that the hyperplasia and hypertrophy of the reticuloendothelial system have not yet been overcome by the treatment. It is, therefore, necessary to watch the patients carefully.

FROM THE AUTHOR'S SUMMARY.

RHEUMATIC FEVER: AN ANALYTIC STUDY OF 73 CASES AT THE HOSPITAL DEL NIÑO. NERI FLORES R., Bol. méd. d. Hosp. inf., Mexico **4**:296 (May-June) 1947.

The incidence of rheumatic fever in Mexico is practically the same as that in other countries which have the same conditions. The symptomatology is the same as that recorded by other authors. In respect to cardiac lesions, the proportion was high, with a predominance of mitral involvements. This high incidence of lesions illustrates the deplorable condition in which these children reached the hospital.

The blood pictures showed a high proportion of erythropenia and leukocytosis, which conditions have also been observed by other investigators. The sedimentation rate was demonstrated to be accelerated in 61 of the 73 cases studied (96.7 per cent), indicating that in these the disease was at it height.

In order to control the active phase of the disease and to insure proper treatment of these patients, electrocardiography has an important place. Sloer and Berezovsky, of Argentina, reported diverse electrocardiographic changes in about 60 per cent of their patients with rheumatic fever. This procedure establishes the diagnosis before audible murmurs are detected.

From the experience obtained with these patients, it is obvious that their stay in the hospital favors the course of the disease. But there are two blank spaces in their treatment: The patients are discharged without being allowed sufficient time for normalization of the sedimentation rate, blood picture and electrocardiogram. There is no effective control of these patients once they are home. These two problems should be conscientiously studied and solved.

Generally speaking, treatment was almost empiric. The only guide was the clinical response of the patient. Unfortunately, the hospital does not have as yet the means to institute digitalis and salicylate treatments with the exactness they deserve. In Coburn's opinion, in order to obtain the best results with salicylates, a blood level of 300 to 350 micrograms should be maintained.

There should be a special department in the hospital for patients with rheumatic fever. This would be a great step forward in the fight on this disease that has recently had such an increased incidence.

FROM THE AUTHOR'S SUMMARY.

Chronic Infectious Diseases

PHALANGITIS SYPHILITIC. FERDINAND DÉMANT and ANDREJ KREMEN, Pediat. listy **2**:253, 1947.

Phalangitis and fibrotic osteomyelitis were observed in a boy 8 months of age. It was difficult to decide whether the conditions were of tuberculous or of syphilitic origin (the father had tuberculosis; the patient showed a positive Pirquet reaction). After antisyphilitic therapy, a rapid and substantial improvement occurred, which, according to the authors, favors a syphilitic origin.

FROM THE AUTHORS' SUMMARY.

SYNDROME OF FROIN IN COURSE OF TUBERCULOUS MENINGITIS. D. G. BONOMI, Policlínico inf. **15**:321 (July) 1947.

The author describes a case of syndrome of Froin in the course of tuberculous meningitis. After relating the clinical history of the case, the author discusses its pathogenesis.

FROM THE AUTHOR'S SUMMARY.

TUBERCULOUS MENINGITIS. OSCAR ILLANES BENITEZ and MARIANO LATORRE BLANCO, Rev. chilena de pediat. **6**:390 (June) 1947.

The authors report the clinical evolution of 2 cases of bacteriologically proved tuberculous meningitis which were treated with streptomycin. Both patients presented active foci of pulmonary tuberculosis. One child 22 months of age received 50 Gm. of streptomycin during two months of treatment, and a girl 13 years of age received 136 Gm. intermittently during five months of treatment. The authors direct attention to these large doses. They were impressed by the efficacy of diluting each 100 mg. of the drug in 5 cc. of spinal fluid when it is employed intrathecally. The dosage, as to amount and frequency of administration, was controlled by weekly chemical and cytologic examinations of the spinal fluid. One of the patients was reported as being clinically well after four months and the other after seven months. The authors report side effects of the drug consisting of radicular pain, severe pruritus, transient strabismus, convulsions and exaggeration of the meningeal signs.

KALISKI, San Antonio, Texas.

TUBERCULIN REACTIONS IN INFANCY AND CHILDHOOD. W. H. OPIE, South African M. J. **21**:740 (Oct. 11) 1947.

Opie discusses the significance of positive reactions to tuberculin tests in children. He reviews the literature and presents two observations on 50 children from a ward for Negroes. Of these 50, 12 gave a positive reaction to tuberculin (1:1000). Two of these had asthma and the reaction was considered of doubtful significance. In the remainder, definite clinical or roentgenologic evidence of active tuberculosis was found. He notes that a positive reaction to a high concentration (1:100) is of doubtful significance.

McGUIGAN, Evanston, Ill.

Diseases of Blood, Heart and Blood Vessels and Spleen

ACUTE ASYSTOLE IN AN INFANT WITH RAPID AND COMPLETE REGRESSION OF THE CARDIOHEPATIC SYNDROME. L. WILLEMIN-CLOG, G. MENUT and L. SADOURNEY, Arch. franç. de pédiat. **3**:319, 1946.

This disorder is observed so infrequently in young children that the most intensive study was made of the patient, a female child 2½ years of age. The onset was sudden, with cough, dyspnea, hepatomegaly and edema of the lower

extremities. After her admission to the hospital, edema was generalized and ascites became severe. There was tachycardia without gallop rhythm or murmur; the blood pressure could not be taken for lack of a suitable cuff. Treatment consisted of absolute rest with a bland salt-free diet, cupping and small doses of digitalis and theobromine. This was augmented in a few days by ouabain—⅛ grain (8 mg.) intramuscularly. Improvement was noted within a few days, and the infant progressed to complete recovery.

AMESSE, Denver.

IDIOPATHIC HYPOPROTHROMBINEMIA AND HEMORRHAGIC DIATHESIS. F. HAUSER, Ann. pædiat. **168**:34 (Jan.) 1947.

A description is given of the symptoms and hematologic findings in idiopathic hypoprothrombinemia caused by inherited factors. The hypoprothrombinemia in these cases cannot be influenced by vitamin K. For that reason, the condition has to be taken into possible consideration when the hepatic test with vitamin K gives a pathologic result.

FROM THE AUTHOR'S SUMMARY.

SULFONAMIDE COMPOUNDS AND AMYLASE IN CHILDREN. A. BOLLETTINO, Rev. di clin. pediat. **44**:702 (Nov.) 1946.

The amylitic ferments of the blood, urine and feces of 50 well children between 3 months and 6 years of age were assayed before and during administration of sulfonamide drugs over a period of four days. The diastase content of the blood serum of each child had gradually decreased—an average amount of 12 per cent the first day, 25 per cent the second day, 39 per cent the third day and 45 per cent the fourth day. Similar decreases were observed in the potency of diastase in the urine and feces. Normal values were obtained again five days after use of the drug had been discontinued.

In vitro experiments were made in which the sulfonamide compound was added to the blood serum of well and of sick children. There was an average diminution of the diastase content of 27 per cent in the serum of the well children and of 34 per cent in that of the sick children.

HIGGINS, Boston.

SERUM IRON IN FAMILIAL ERYTHROBLASTIC (COOLEY'S) ANEMIA. M. AMATO, Riv. di clin. pediat. **44**:711 (Nov.) 1946.

The iron content of the blood serum of 6 children with familial erythroblastic (Cooley's) anemia was 114, 138, 180, 184, 196 and 210 γ per hundred cubic centimeters. Normal values are between 77 and 97 γ per hundred cubic centimeters. In view of no extraordinary excretion of urobilinogen, it would appear that there is inadequate utilization of the iron by the marrow cells.

HIGGINS, Boston.

CHANCES OF SURVIVAL IN VON JAKSCH-HAYEM-LUZET ANEMIA. G. CAREDDU, Riv. di clin. pediat. **44**:721 (Dec.) 1946.

The author, after briefly summing up the evolution of medical knowledge on familial erythroblastic (Cooley's) anemia, calls attention to the fact that in differential diagnosis one can still speak of Von Jaksch-Hayem-Luzet splenic anemia only in those cases in which familial erythroblastic anemia, as well as Di Guglielmo's erythroblastosis, can be excluded. Notable contributions to differential diagnosis are determinations of hemolytic resistance and red blood cell measurements, as even in initial and vague cases these data provide sufficient proof to substantiate other clinical findings.

FROM THE AUTHOR'S ABSTRACT.

SYMMETRIC SPHACELUS OF THE SKIN IN SCHÖNLEIN-HENOCH PURPURA. A. SEGERS and A. J. BORDENAVE, Arch. argent. de pediat. **26**:265 (Oct.) 1946.

This is a report of a case, which according to the author, is a sympatheticotonic vasal trophoneurosis, toxic in origin.

ROJAS, Boston.

INVESTIGATIONS ON HEMOPHILIA: VII. HUMAN PLASMA FRACTIONS IN HEMOPHILIA. S. VAN CREVELD and G. G. A. MASTENBROEK, Acta brev. Neerland. **14**:51, 1946.

This research is a continuation of investigations on the treatment of hemophilia by a substance prepared from human plasma which promotes coagulation. The amount of coagulation was determined in venous blood at 37 C. (98.6 F.). A "fibrinogen," prepared by the Lister Institute in London by their method of ether fractionation, was dissolved in pyrogen-free water in such a way that it gave a 1.5 to 2 per cent solution. This solution, injected intravenously, greatly reduced the coagulation time, which retardation persisted for a considerable period. After repeated injections, no disagreeable reactions were seen and no refractory period was observed. It is not known whether this activity depends on a protein or on some substance attached to a protein.

FROM THE AUTHORS' SUMMARY.

SURGICAL TREATMENT OF PATENT DUCTUS ARTERIOSUS (BOTALLI). L. D. EERLAND, Nederl. tijdschr. v. geneesk. **90**:560 (June 1) 1946.

This is a report of a case, with discussion of the problem.

VAN CREVELD, Amsterdam, Netherlands.

CURE OF ENDOCARDITIS LENTA WITH PENICILLIN. J. E. MINKENHOF, P. FORMYNE and H. A. P. HARTOG, Nederl. tijdschr. v. geneesk. **90**:604 (June 8) 1946.

From recent publications it appears that endocarditis lenta can be cured in 75 per cent of cases by means of penicillin, if it is given in large doses (at least 200,000 units daily) and over a long time (four to eight weeks). Treatment should be continued until all symptoms of sepsis (enlargement of the spleen, emboli and pains in the joints) has disappeared. Moderate fever does not mean that recovery is not occurring but may be a consequence of the treatment with penicillin.

In 2 severe cases successful treatment with penicillin is reported. In a third case, reported only briefly, the micro-organism responsible (in all 3 cases, Streptococcus viridans) was extremely resistant to penicillin.

VAN CREVELD, Amsterdam, Netherlands.

VARIABILITY OF SERUM BILIRUBIN DURING TWENTY-FOUR HOURS IN NORMAL CHILDREN. S. WENDT, Nord. med. (Hygiea) **29**:245 (Feb. 1) 1946.

Forty-three children, 3 months to 10 years of age, were examined (by the micro method of Jendrassik, Gröf and With) eight to ten times daily. It was observed that the level of serum bilirubin in the morning (0.37 mg. per hundred cubic centimeters) is 30 per cent higher than in the evening (0.26 mg. per hundred cubic centimeters). This difference is statistically significant.

WALLGREN, Stockholm, Sweden.

BLOOD VALUES IN HEALTHY INFANTS TREATED WITH IRON. KJELL L. MÖLLER and BO VAHLQUIST, Nord. med. (Hygiea) **30**:1101 (May 17) 1946.

The authors tried in vain to raise the comparatively low average values for hemoglobin concentration (12 to 12.5 Gm. per hundred cubic centimeters), color index (0.85) and serum iron (85 micrograms per hundred cubic centimeters) in

children during the second half-year of life and during the years immediately following by giving them large doses of reduced iron. They conclude that these low values apparently must be looked on as a physiologic phenomenon typical of children of that age.

WALLGREN, Stockholm, Sweden.

Diseases of Nose, Throat and Ear

DOES MILK "MAKE MUCUS"? RAY M. MOOSE, California Med. **68**:31 (Jan.) 1948.

Reports from more than 600 patients have indicated that milk is not the cause of annoying postnasal mucus. The causation of this common disturbance needs further investigation. Milk is too valuable a food to be omitted from the diet because of the popular belief that "milk makes mucus."

PRYOR, Redwood City, Calif.

STUDIES ON THE TRANSMISSION AND CONTROL OF RESPIRATORY DISEASE WITHIN ARMY BARRACKS: I. HEMOLYTIC STREPTOCOCCAL CONTAMINATION OF THE ENVIRONMENT. C. G. LOOSLI, H. M. LEMON, H. WISE and O. H. ROBERTSON, J. Infect. Dis. **82**:59 (Jan.-Feb.) 1948.

From December 1943 to August 1944, a bacteriologic study was made of dust from floors, beds, wearing apparel and air in barracks, at Camp Carson, Colo. Particular attention was paid to the beta hemolytic streptococcic content. The streptococcic contamination of the barracks was low during the winter and summer and high during the spring.

Persons with noses and throats giving positive cultures for hemolytic streptococci showed far greater numbers of the corresponding types in their bedding than did those with these organisms present only in their throats. In the barracks in which the majority of the positive cultures from bedding, dust and air showed the same type of streptococcus, this same type was most prevalent in the positive nose and throat cultures of the barrack personnel.

The greatest number of positive air cultures was obtained in barracks in which the beds and floor dust were heavily contaminated with hemolytic streptococci. The highest streptococcic counts per cubic foot of air and the most frequently positive cultures were obtained during the time of maximum activity, such as getting up, dressing, floor sweeping and bed making. The extensive and uniform contamination of the beds and floor dust can be explained adequately only on the basis of the aerial spread of those organisms throughout the barracks.

TOOMEY, Cleveland.

THE TRANSMISSION AND CONTROL OF RESPIRATORY DISEASES IN ARMY BARRACKS: II. THE SPREAD OF HEMOLYTIC STREPTOCOCCAL INFECTIONS AMONG ENLISTED PERSONNEL. H. M. LEMON, C. G. LOOSLI and M. HAMBURGER JR., J. Infect. Dis. **82**:72 (Jan.-Feb.) 1948.

A study of some of the factors involved in the spread of streptococcic infections of the respiratory tract among seasoned men and new inductees was made at Camp Carson, Colo., from March 1 to Aug. 1, 1944. The rate of admissions to the hospital for nasopharyngitis among the seasoned personnel was 10.6 per cent. Sixty-four per cent had throat cultures positive for beta hemolytic streptococci. Admissions from two companies of new recruits were higher (21 per cent), although in only 37 per cent of these patients did material from the throat yield streptococci.

In certain periods admission rate for patients with streptococcic infections with a single type of organism from several platoons was high enough to be considered epidemic in proportion to their strength, although cases due to similar types did not occur among the personnel of the other platoons of the same or other companies.

Four instances were reported which illustrate the remarkable capacity of persons to contaminate their barracks environment, some over a long period of time. The important role played by a nasal disperser (dangerous carrier) for types 30 and 46 of beta hemolytic streptococci in contaminating the environment, resulting in outbreaks of streptococcic disease among the occupants of barracks, is described.

From the Authors' Summary.

Evaluation of Ultraviolet Radiation and Dust Control Measures in Control of Respiratory Disease at a Naval Training Center. W. R. Miller, E. T. Jarrett, T. L. Willmon, A. H. Hollaender, E. W. Brown, T. Lewandowski and R. S. Stone, J. Infect. Dis. **82**:86 (Jan.-Feb.) 1948.

Uultraviolet irradiation of the floors and upper air in barracks housing recruits resulted in a 19.2 per cent over-all reduction in total respiratory disease. Streptococcic disease rates were at a high level and a 24 per cent reduction was obtained. The reduction was fairly constant throughout the season. There was no consistent difference in percentage reduction when the rates were highest.

Dust control measures gave variable results on rates for respiratory disease throughout the season. The over-all analysis showed no reduction in the incidence of rates for respiratory disease in the dust control group.

The total bacterial and streptococcic content of the air and the total bacterial content of blanket dust and floor dust were significantly reduced by both dust control and ultraviolet irradiation. The streptococcic content of floor dust and the rate of streptococcus carriers were not changed. The lack of parallelism between bacterial incidence in the environment and rates of respiratory disease is emphasized.

From the Authors' Summary.

The Treatment of Acute Respiratory Infections in Children with Orally Administered Unbuffered Penicillin Solution. W. S. Hoffman, J. W. Hoffer and H. Gordon, J. Pediat. **32**:1 (Jan.) 1948.

A preliminary study of 209 infants and children given single doses of unbuffered crystalline potassium penicillin G revealed that doses of 10,000 to 20,000 units for infants under 1 year of age and approximately 3,000 units per kilogram of body weight thereafter resulted in satisfactory therapeutic penicillin concentration in the plasma. One hundred and forty-three children with acute infections of the upper respiratory tract were then treated orally with the same penicillin preparation every three hours according to the following dosage schedule: 0 to 1 year of age, 20,000 units; 1 to 4 years, 40,000 units; 4 to 6 years, 60,000 units; 6 to 10 years, 80,000 units; 10 to 12 years, 100,000 units.

A preliminary dose equal to twice the therapeutic dose initiated the therapy. Three hour plasma levels were measured and reported to average 0.03 to 0.05 unit per cubic centimeter. Good results were obtained in 65.7 per cent of the patients treated and fair results in 18.2 per cent. Good results were defined as subsidence of fever with clinical improvement within twenty-four hours. The authors recommend increasing the oral dosage or the amount of penicillin given parenterally if no response occurs in forty-eight hours.

Grulee Jr., Galveston, Texas.

INFANT SPEECH: DEVELOPMENT OF VOWEL SOUNDS. ORVIS C. IRWIN, J. Speech & Hearing Disorders **13**:31 (March) 1948.

Analysis of the percentage of total occurrence of vowel sounds in each of fifteen age levels at two month intervals shows that while most of the vowel sounds are used by young infants, only three of them, the front vowels, e as in set, i as in sit and the middle vowel, u as in sun, are consistently used by infants at the first age level of 1 to 2 months. The newborn infant's vowel sound repetoire is decidedly unlike that of the adult. There is an infant vocalization or preponderance of front and middle vowel utterance during the first year which thereafter gradually diminishes, while back vowels increase until at 2½ years the percentage distribution approximates that of the adult without, however, being identical with it.

PALMER, Wichita, Kan.

MAKE MOTHER A CLINICIAN. HEROLD LILLYWHITE, J. Speech & Hearing Disorders **13**:61 (March) 1948.

Speech clinics generally pay too little attention to parents in the development of clinician programs. The author is of the opinion that 4 of 5 mothers can be made useful in the development of the child, particularly in those with the more serious types of conditions. Mothers are taught to use all the avenues of stimulation, visual, auditory and kinesthetic, as well as smell, taste, touch and color. Object-symbol association is taught to the mother. For example, she teaches the word "walk" by walking vigorously within the child's range of vision as she repeats the word over and over again. Carefully selected reading material is given the mother to study.

PALMER, Wichita, Kan.

FUNDAMENTALS IN THE TREATMENT OF COMMUNICATIVE DISORDERS CAUSED BY HEARING DISABILITY, PART II. MIRIAM D. PAULS and WILLIAM G. HARDY, J. Speech & Hearing Disorders **13**:97 (June) 1948.

The treatment of communicative disorders caused by hearing disability involves the closest coordination of medical and nonmedical services. Complete diagnostic evaluation includes an otologic examination, a full series of hearing tests, psychoacoustic and psychosocial examination and a thorough case history. Special attention is paid to the patient's communicative habits and to his attitudes and behavior in typical communicative situations.

The terms "deaf" and "hard of hearing" and similar designations are not physiologically sound. It is convenient to think of such losses in terms of marginal, moderate and profound hearing loss. Of almost 5,000 service personnel and veterans with hearing disabilities known to the authors, fewer than a dozen were so affected that they could not profit from the use of a hearing aid and from retraining with amplified sound. The group with mild loss of hearing had the greatest difficulty in adjusting to the communicative problems.

Several guide lines must be followed in working with persons with hearing disabilities. First, the doubts, confusions and questions of the handicapped person must be faced squarely. Second, the person must have ample opportunity ot learn to listen to amplified sound, to center his attention in ambient noise, to extend the limits of his tolerance for loud sound, and to utilize every possible auditory cue. Third, once the hearing aid of choice has been determined, the person must learn to use it in a wide variety of situations. Fourth, the patient must understand the role of speech reading. Fifth, there should be sufficient instruction in the fundamentals of articulation and of voice production to insure the retention of adequate habits. Sixth, problems of psychosocioeconomic adjustment need free discussion.

PALMER, Wichita, Kan.

THE WISH FOR DEFECTIVE SPEECH. NORMAN W. FREESTONE, J. Speech & Hearing Disorders **13**:119 (June) 1948.

Behavior is the product of wishes. Speech is a function of behavior which aids materially in securing the wants of the organism. The majority of qualified speech clinicians consider in their approach that they are dealing with a speech-defective person rather than with a speech defect. The dropping of speech symptoms before one is emotionally ready for their removal will either increase the anxiety of the patient or force him to compensate in other directions. The speech act, no matter how it functions, represents a certain level of ego control. It would be well to cultivate speech as a symbol of psychotherapeutic value.

PALMER, Wichita, Kan.

SUPPLEMENTARY TECHNIQUE TO USE WITH SECONDARY STUTTERERS. RUTH M. CLARK, J. Speech & Hearing Disorders **13**:131 (June) 1948.

One aspect of therapy for stuttering is usually concerned with mental hygiene. Nondirective counseling in group situations and individually written autobiographies are proposed as supplementary methods to be used with secondary stutterers as a means of gaining good mental hygiene.

PALMER, Wichita, Kan.

ANALYSIS OF SPEECH CORRECTION WORK BY STATES [THIRD REPORT]. MARTIN F. PALMER, J. Speech & Hearing Disorders **13**:151 (June) 1948.

Distribution of professional services in the states shows generally that the opportunities are still great. Two states as yet have no adequate speech corrective services. These are Arkansas and New Mexico. Generally, the eastern states have poorer programs than the midwestern states.

PALMER, Wichita, Kan.

INFECTIOUS CROUP: I. ETIOLOGY. EDWARD F. RABE, Pediatrics **2**:255 (Sept.) 1948.

This report is based on a study of 347 cases of infectious croup. Infectious croup is defined as a disease of the upper part of the respiratory tract characterized by inflammation of the rhinopharynx with downward spread of the infection, leading to variable degrees of stenosis of the laryngeal, laryngotracheal or laryngotracheobronchial air passages. This stenosis is due to edema and is occasionally aggravated by formation of membrane.

On the basis of recognized signs and symptoms, infectious croup has been divided into three clinical groups, namely, laryngitis, laryngotracheitis and laryngotracheopneumonitis. Such a classification proved to have prognostic, but not etiologic, significance for the individual case. By correlation of the bacteriologic and pathologic aspects and clinical course of the present cases, infectious croup was divided into three distinct etiologic categories, namely diphtheritic croup, Hemophilus influenzae type B croup and so-called virus or nonbacterial croup.

FROM THE AUTHOR'S SUMMARY.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

CORROSIVE ESOPHAGITIS IN CHILDREN. R. V. PLATON and G. J. AUSTIN, New Orleans M. & S. J. **101**:284 (Dec.) 1948.

A survey of children admitted to the Charity Hospital, New Orleans, with corrosive esophagitis over a period of six years reveals a poor record therapeutically. It is the authors' opinion that these results could be materially improved

by more careful study of the individual patient. It should be possible within thirty days to decide which patients should be given prolonged treatment and which can be discharged from the hospital with instructions to return if difficulty in swallowing develops. Earlier surgical intervention may be justified when it is obvious that parental cooperation for at least six months in the outpatient department will not be obtained. It is suggested that earlier anastomosis rather than prolonged attempts at dilation following gastrostomy may lower the present high mortality rate.

McGUIGAN, Evanston, Ill.

TREATMENT OF INFANTILE DIARRHEA WITH STREPTOMYCIN AND AN ORAL AMIGEN MIXTURE. ELVIRA GOETTSCH, GEORGE COBLEY and MARY MULLOY, Pediatrics **2**:1 (July) 1948.

In a severe epidemic of infantile diarrhea in 1945 and subsequently, bacteriologic cultures of material from the nasopharynx and of the catheterized urine showed a predominance of gram-negative organisms of the colobactrum group.

The response of seriously ill infants with parenteral diarrhea to streptomycin was dramatic, presumably because of the specific action of the drug against the gram-negative organisms. Streptomycin was used both orally and intramuscularly in the later stages of the disease.

Suggestions are offered for fluid and electrolyte replacement by means of oral use of a mixture of protein hydrolysates (amigen®), which permits the introduction of potassium, calcium and nitrogen, as well as sodium and chloride, by mouth shortly after the infant's admission.

The use of streptomycin and the amigen® mixture orally, as an adjunct to the customary routine employed in previous years, effectively shortened the stay in the hospital, decreased the amount of therapy given intravenously and reduced the mortality. During the eight month period of observation no deaths were encountered which could be attributed to diarrhea.

FROM THE AUTHORS' SUMMARY.

THE RELATIONSHIP OF FIBROCYSTIC DISEASE OF THE PANCREAS TO A DEFICIENCY OF SECRETIN. ARCHIE H. BAGGENSTOSS, MARSCHELLE H. POWER and JOHN H. GRINDLAY, Pediatrics **2**:435 (Oct.) 1948.

Theories which indicate that fibrocystic disease of the pancreas results from a congenital deficiency of secretin are outlined. The varied clinical and pathologic manifestations of this disease can be more nearly adequately explained by this hypothesis than by any other current theories. The absence of secretin in the upper part of the intestinal tract of a patient with the disease supports this theory, i. e., that the condition results from a congenital deficiency of secretin.

It is possible to extract secretin from the upper portion of the intestinal tract of persons 2 months to 73 years old. Consistent failures occurred only in those in the neonatal period. Successful extraction of secretin from these patients can be done by combining the crude extracts obtained from a number of patients. The extraction of secretin is successful if done up to fifteen hours post mortem. If the specimen is frozen, extraction can be delayed up to thirty-nine days without loss of activity. Because this method of extraction is successful in individual cases at necropsy, it becomes possible to correlate the presence or absence of secretin with varying pathologic conditions. This may open a broad field for the investigation of many pancreatic and intestinal disturbances, in addition to fibrocystic disease of the pancreas.

FROM THE AUTHORS' SUMMARY.

ACUTE DIARRHEA IN INFANCY. ANIBAL ARIZTIA and CARLOS GARCÉS, Pediatrics **2**:525 (Nov.) 1948.

An analysis of acute diarrheas in infancy was made, based on the clinical study of two groups of children: the first consisted of 3,391 diarrheal episodes in 1,505 infants in a period of six years and the second, of 199 children who had a dysentery-like diarrhea in a period of one year's observation. Of those 3,391 diarrheal episodes, we found that 3,020 had a parenteral origin, 210 had an enteral causation and 161 were caused by no demonstrable infection. We consider every acute diarrheal episode in infancy to have an infectious origin, either from parenteral causes or from specifically enteric exogenous germs, as well as the nonspecific intestinal flora.

In the great majority of our cases of diarrhea (2,060, or 60.7 per cent) there was a coexisting metabolic impairment. This was almost general in the group with enteral infection, having a mortality rate of 17 per cent. The isolation of a specific enteric germ (salmonella and shigella) was possible in only approximately 30 per cent in both groups, the first with 210 cases of enteral infection, and the other with 199 children having dysentery-like diarrhea. Our highest incidence of diarrhea was in spring and summer. Most of the affected children were previously undernourished.

Postmortem examinations in fatal cases failed to show a relation between the severity of intestinal lesions and the type and origin of the infections. Nor could we demonstrate a definite parallelism between cause and character of the diarrhea, although specific enteric infections had a certain predominance in the inflammatory stools (salmonella and shigella).

From a diagnostic, therapeutic and prophylactic standpoint, we noted two important elements in any given case of diarrhea: its metabolic impairment and the infectious etiologic factor. We think neither element alone justifies the denomination and classification of acute diarrhea in infancy.

The preservation of a good nutritional state and the sanitary control of food, water and sewage, as well as the elimination of carriers, seem to be of the foremost prophylactic importance. In the individual case treatment should correct the metabolic impairment and eliminate the infection.

FROM THE AUTHORS' SUMMARY.

AN OUTBREAK OF NAUSEA, VOMITING AND DIARRHEA ON A MATERNITY SERVICE; TRANSMITTED TO A CHILD CARING INSTITUTION AND TO PRIVATE HOMES. HAROLD ABRAMSON and HAROLD T. FUERST, Pediatrics **2**:677 (Dec.) 1948.

An outbreak of epidemic nausea, vomiting and diarrhea in newborn infants is described. The communicability of the disorder is demonstrated by its direct spread to the residents of a child-caring institution and the occupants of a nearby tenement house. We are in agreement with the observations of Brown, Crawford and Stent and those of Cook and Marmion that the condition is a relatively mild one in newborn infants and that it should not be confused either clinically or epidemiologically with the syndrome of epidemic diarrhea of the newborn.

A differential diagnosis, based on clinical and epidemiologic factors, should be made between this disorder and epidemic diarrhea of the newborn, salmonella infection of the newborn and the diarrhea accompanying stomatitis in young infants.

Outbreaks in nurseries for newborn infants should be studied carefully and indiscriminate grouping of cases avoided. Distinctive and constant clinical and epidemiologic features should be sought in each outbreak to separate it from the general group of diarrheal disorders of the newborn.

FROM THE AUTHORS' SUMMARY.

CONGENITAL ANKYLOGLOSSIA (TONGUE-TIE) ASSOCIATED WITH GLOSSOPTOSIS (RETRUDED MANDIBLE) AND PALATUM FISSUM (CLEFT PALATE). HANS MAY and LIN T. CHUN, Pediatrics **2**:685 (Dec.) 1948.

A case of congenital tongue-tie, associated with retruded mandible, glossoptosis and cleft palate in a newborn infant is discussed. Similar cases of the so-called Pierre Robin syndrome have been described, but in none has there been an associated ankyloglossia. The tongue-tie was so prominent that the tip of the tongue was bent acutely downward and backward and was buried in the floor of the mouth. The infant had frequent attacks of difficulty in swallowing, dyspnea and cyanosis, which threatened his life. To relieve the difficulty in breathing and swallowing, two emergency tracheotomies were performed.

Two operative procedures were done to correct the tongue-tie. The first freed the tip of the tongue by a V-shaped incision on either side. The second further lengthened the tongue by a Z-plasty incision at its base where the frenulum normally would be situated.

After the operations, the infant gradually improved, and by "orthostatic feeding" he was able to feed normally and to breathe without difficulty at the age of 3 months.

FROM THE AUTHORS' SUMMARY.

JUVENILE CIRRHOSIS. URSULA JAMES, Proc. Roy. Soc. Med. **40**:162 (Feb.) 1947.

The patient, 7¼ years of age on her admission to the hospital, was found to be backward in walking and talking and had been taking ½ grain (0.03 Gm.) of thyroid extract daily for four years. Her weight was 4 stone 3 pounds (26.8 Kg.) Physical examination revealed dark skin, a firm liver 2 fingerbreadths below the costal margin and the spleen firm and enlarged to the umbilicus. The Wassermann reaction was negative. Sternal puncture showed normoblastic marrow and no Gaucher's cells. She was discharged from the hospital with her condition undiagnosed, to continue taking ½ grain of thyroid daily. Two months later she was readmitted, and tonsillectomy and adenoidectomy were performed. She was discharged after an uneventful convalescence. She was again admitted a month later on account of spontaneous bruising of the limbs. A systolic apical murmur was noticed. The patient was hot, sweating and emotional and had tantrums. Gain in weight was rapid without use of thyroid, which was again commenced. Later examination showed exophthalmos, a fine tremor of the hands and presence of von Graefe's sign. A biopsy specimen of the skin showed an intense melanin deposit in basal layers and no hemosiderin; blood cholesterol was 258 mg. per hundred cubic centimeters; the van den Bergh reaction was delayed and weakly positive. A laparotomy was performed and the spleen was observed to be smooth, vascular and enlarged to the umbilicus. The liver was small and hard with a rounded margin. Her convalescence was uneventful. Results of the biopsy of the liver and a discussion on the pathologic observations and diagnosis are also given in the report.

WILLIAMSON, New Orleans.

HEPATOSPLENOMEGALY: FOR DIAGNOSIS. PHILIP EVANS, Proc. Roy. Soc. Med. **40**:163 (Feb.) 1947.

A case of hepatosplenomegaly was reported in a boy 4 years 10 months of age. The spleen reached the left pubic ramus; the liver was enlarged 2 fingerbreadths below the costal margin, and there was generalized glandular enlargement. The results of the investigations made accompany the report.

WILLIAMSON, New Orleans.

LETHAL HEPATOSIS. A. A. BONDUEL, A. A. GIUSSANI and M. E. JÖRG, Arch. argent. de pediat. **27**:8, 1947.

This is a report of 2 cases. The clinical histories are included. The term hepatosis is used for a number of hepatic diseases, among which so-called catarrhal jaundice is included. The severe forms of hepatosis can be classified as: (1) lethal acute hepatitis, the true acute, red-yellow atrophy, the evolution of which is always fatal and (2) subacute hepatosis, a more benign form that allows three to four weeks' survival, according to Herxheimer. The repetition of this form leads to the condition Paltauf called "relapsing hepatic atrophy" or to the "regenerative nodular hyperplasia" of Marchand.

The subacute form has a relatively insidious onset, although the onset occasionally resembles that of the acute form and sometimes presents moderate ascites, edema of the lower extremities and distinct icterus. The liver decreases progressively in size, while the spleen increases. Histologically, the liver shows patchy areas of cellular degeneration some of which have been replaced by dense connective tissue that may become as compact as that of a cirrhosis. The clinical severity depends on the changes of the binomial necrosis and regeneration. The transformation of a catarrhal jaundice or a hepatitis into subacute hepatic atrophy is manifested most commonly by a constant and fixed pain in the right upper quadrant. The terminal event is, as a rule, an added infectious process, frequently a respiratory infection.

The urine is hyperpigmented, with abundant albumin. The performance of hepatic function tests is not necessary for the diagnosis or the prognosis of the disease. The evolution is toward hepatic insufficiency and coma.

A discussion of bilirubinemia and the various ways in which it is interpreted is given. The authors consider the increase of bilirubinemia at the expense of indirect bilirubinemia a sign of poor prognosis. Pathologic changes are enlargement of centrolobular veins; necrotizing degeneration of the center of the lobules with trabecular disarrangement and reticular hyperplasia and infiltration with lymphocytes, monocytes and plasma cells. The degenerative changes are minimal in the portal spaces. In the kidneys there are cloudy swelling and vacuolization of the cells of the lobules. Albumin and bile casts are present. The glomeruli are not remarkable.

ROJAS, Boston.

APPENDICITIS DUE TO A FOREIGN BODY IN A SEVEN MONTH OLD CHILD. A. MARANO, J. DAMIANOVICH and A. VIDAL FREYRE, Arch. argent. de pediat. **27**:55, 1947.

This is a report of a case. The appendix contained a shoemaker's nail. Other cases from the literature on appendicitis due to a foreign body are mentioned.

ROJAS, Boston.

Nervous Diseases

HYDROCEPHALUS: A CONTRIBUTION RELATED TO TREATMENT. OLAN R. HYNDMAN, J. Neurosurg. **3**:426 (Sept.) 1946.

Hyndman previously reported on 4 cases of hydrocephalus treated by choroid plexotomy. The operation consists in evulsion of the choroid plexus at the glomus, thus establishing communication between the lateral ventricles and the subarachnoid space through disruption in the laminas of the choroid plexus. In the author's opinion, an opening in the region is less likely to be obliterated by normal healing processes.

He again reports on the 4 cases and adds a fifth. In 3 cases of congenital hydrocephalus treatment was with ventriculocisternostomy. In all cases the hydro-

cephalus was relieved. In 2 cases death occurred from nonsurgical causes and in 1 case the patient was still in excellent condition at the time of writing, with no increase in size of the head. In 1 case, that of a man with chronic arachnoiditis and resulting hydrocephalus, the patient was treated in the same way and two months later had normal ventricular pressure. In the fifth case, that of a 7 year old girl with hydrocephalus following pneumococcic meningitis and adhesive basal arachnitis, choroid plexotomy was performed. Twenty-one months later (January 1946) she had normal spinal fluid pressure with complete regression of her previous papilledema.

Hyndman concludes that this procedure provides a simple and most effective means of treating congenital and acquired hydrocephalus, both of the communicating and of the noncommunicating type.

TOZER, Philadelphia [ARCH. NEUROL. & PSYCHIAT.].

LYMPHOCYTIC MENINGITIS WITH LUNG INVOLVEMENT OCCURRING IN CHILDHOOD. JOHN APLEY, Arch. Dis. Childhood **22**:18 (March) 1947.

An account is given of virus disease producing lymphocytic meningitis and pneumonia simultaneously. It is suggested that the rarity of this coincident involvement of two systems is more apparent than real.

The diagnosis of lymphocytic meningitis with atypical pneumonia, presumably due to virus infection, was made in 3 cases occurring in children.

KELLY, Milwaukee.

ANGIOMA OF THE BASAL GANGLIA. DONALD PATERSON and WYLIE MCKISSOCK, Proc. Roy. Soc. Med. **40**:164 (Feb.) 1947.

A case of angioma of the basal ganglions is reported in a boy 9 years of age.

WILLIAMSON, New Orleans.

INTRACRANIAL HAEMANGIOMA CAUSING CONVULSIONS. M. W. WEST, Proc. Roy. Soc. Med. **40**:164 (Feb.) 1947.

The patient, a boy 9 years of age, was admitted to the hospital with convulsions for the past eighteen months, which were increasing in frequency. No abnormal physical signs were found beyond a tendency to left internal deviation. In the roentgenologist's opinion the appearance of the skull suggested intracranial hemangioma (left). It was proposed to treat this condition with roentgen radiation.

WILLIAMSON, New Orleans.

ENCEPHALITIS IN A CHILD. D. N. CHATTERJI and K. C. CHAUDHURI, Indian J. Pediat. **14**:122 (July) 1947.

A case of encephalitis in a 3 year old child is discussed, with detailed observations and notes on treatment and progress. The child recovered after eighty-eight days of unconsciousness. A brief classification of the encephalitides is included.

MCGUIGAN, Evanston, Ill.

TREATMENT OF OBSTRUCTIVE HYDROCEPHALUS IN INFANTS BY OPENING THE LAMINA TERMINALIS. JEAN GUILLAUME and CHARLES RIBADEAU-DUMAS, Rev. neurol. **77**:173 (July-Aug.) 1945.

The authors report their experiences with the construction of an opening in the lamina terminalis, or the anterior wall of the third ventricle, in treatment of obstructive hydrocephalus. They report successful operations on 3 infants, 11, 6

and 3 months of age, respectively. The operations were performed with the use of local anesthesia. Two or three days before the operation ventricular drainage was carried out by means of puncture through the anterior fontanel. Such drainage facilitates adaptation of the brain to the altered hydrodynamic situation following the opening of the lamina terminalis. The authors suggest making a small puncture at first to allow the spinal fluid to flow slowly out of the ventricle; the opening is later enlarged. During the operation the ventricles are filled with Ringer's solution to prevent sudden collapse of the cerebral hemispheres. The operation in all 3 cases was successful so far as the enlargement of the head was concerned; in 1 case the head became smaller, and in another the child, who was blind, was able to see again. SAVITSKY, New York [ARCH. NEUROL. & PSYCHIAT.].

TONIC REFLEXES DUE TO ROTATION OF HEAD ON TRUNK AND OF BODY IN HORIZONTAL PLANE: THEIR INFLUENCE ON PLANTAR REFLEXES. ENZO LIESCH, Riv. clin. pediat. **45**:411, 1947.

The changes in position of the head in relation to the trunk and of the body in relation to the horizontal plane in children in physiologic condition from birth to the age of 3 years modify the original plantar reflexes.

The modifications, which are individually characteristic, consist in inversion, inhibition or accentuation of the reflex. The modifications are necessarily independent of the fact that change in position of the head or trunk may or may not cause characteristic tonic reflexes (cervical and labyrinthine) to appear in the extremities.

The observed phenomena are to be interpreted as the illustration of important facts of facilitation and inhibition.

Therefore, from a general point of view, reflexes or nervous impulses having a tonic character modify phasic reactions in a limited muscular area, a fact which generally is not considered in the study of tonic reactions.

FROM THE AUTHOR'S SUMMARY.

USE OF CARBOGEN IN ENCEPHALOGRAPHIES IN CHILDREN. F. ESCARDÓ and P. O. SAGRERAS, Arch. argent. de pediat. **27**:3, 1947.

Carbogen is a mixture of 95 parts oxygen and 5 parts carbon dioxide. The authors consider the use of this mixture far superior to the employment of air in encephalography. Two cases are presented in which large amounts of carbogen® were tolerated by the patient without any inconvenience, while lesser amounts of air produced fever, cephalic pain, vomiting, profuse sweating and bradycardia.

They conclude that the use of carbogen® should definitely replace the use of air in encephalography.

ROJAS, Boston.

HEMOPHILUS INFLUENZAE MENINGITIS. JULIO MENEGHELLO and GLADYS SUDZUKI H., Rev. chilena de pediat. **7**:20 (Jan.) 1947.

The authors report 5 cases of Hemophilus influenzae meningitis, treated by a combination of penicillin and sulfonamide drugs. Their mortality was 40 per cent. Inasmuch as streptomycin was not available to them, they advise the employment of penicillin, when penicillin sensitivity of the causal organism can be demonstrated.

KALISKI, San Antonio, Texas.

MENINGITIS IN YOUNG INFANTS DUE TO SAPROPHYTIC BACTERIA OF THE INTESTINE. PEDRO OYARCE ROJAS, Rev. chilena de pediat. **8**:527 (Aug.) 1947.

The author reports 8 cases of meningitis in infants less than 2 months of age. In 5 of these the organism was Proteus vulgaris; in 1, Proteus mirabilis, and in 2, Escherichia freundii. The predominant symptoms were fever, convulsions, vomiting, tenseness of the fontanel and, in some instances, separation of the cranial sutures. The author emphasizes the serious nature of infections of this character and comments on the ineffectiveness of penicillin and sulfonamide derivatives, the use of which is commonly followed by hydrocephalus if death does not result. In the opinion of the author, streptomycin is the drug of choice in this variety of meningitis.

KALISKI, San Antonio, Texas.

THE SPINAL REFLEX OF GALANT. I. FLESCH, Paediat. danub. **2**:64 (Aug.-Sept.) 1947.

The response to Galant's reflex in nearly 100 infants was observed. Contrary to the original description, the reflex was elicited with the hand instead of with a hammer. It was observed that pressure exerted on any part of the reflexogenic area sufficed to evoke the reflex. With the technic used, it became possible to elicit the reflex in the prone position in older children. This, according to the author, corresponds to the tickle reflex of adults.

The method of examination used led to the observation of a reflex which has not yet been described and which was named the lordotic spinal reflex. It can be elicited by running two fingers along both sides of the spine. The infant responds with lordosis, elevation of the pelvis, the thighs and the knees taking a sitting position. The arms are adducted and head tilted back.

The author considers that this phenomenon originates from the superposition of two Galant reflexes. Further observations are necessary to establish whether one could conclude from the hyperactive appearance of this reflex that pathologic states of the nervous system exist.

FROM THE AUTHOR'S SUMMARY.

Psychology and Psychiatry

DEVELOPMENTAL PEDIATRICS: ITS TASK AND POSSIBILITIES. ARNOLD GESELL, Pediatrics **1**:331 (March) 1948.

The practice of pediatrics in America includes normal, as well as sick, defective and handicapped children. Development, as well as disease, comes within the responsibility of the pediatrician and family physician. Parents are interested not only in the physical health but in the mental health of the growing child. They are constantly asking for advice and guidance on the best methods of care and training, whether the child is normal, backward or handicapped. The task of clinical pediatrics is to meet these increasing demands for a broader type of child protection. Protection must begin with nutrition and physical welfare, but it can be extended to include mental welfare.

Developmental pediatrics is especially concerned with the evaluation and supervision of child development at periodic intervals, so that the total development can be medically safeguarded and fostered. Development manifests itself not only in physical signs but in patterns of behavior. The behavior patterns undergo growth changes. The changes can be evaluated through appropriate behavior tests which reveal the maturity and the efficiency of the nervous system.

Systematic developmental examinations of infant behavior are particularly important in the first three years of life. These first years are the most favorable

for establishing mental health and for promoting wholesome relationships between parent and child. This also is the critical period for discovering defects and deviations—visual and auditory handicaps, motor disabilities, cerebral injuries, retardation and personality difficulties.

Early diagnosis leads to improved methods of treatment and guidance. Clinical pediatrics is in a strategic position to take over this extensive field of preventive mental hygiene. The methods of developmental diagnosis should be incorporated into general pediatrics but must also be applied at a more specialized level in regional health centers and teaching hospitals.

Developmental methods of diagnosis and supervision constitute the basis of a workable infant and child psychiatry. At a specialized level, developmental pediatrics becomes a new form of clinical infant psychiatry greatly needed for the differential diagnosis of complex cases of defect and deviation. The broadest task of developmental pediatrics, however, is in the vast field of preventive mental hygiene, which embraces the multitude of normal and near normal children.

FROM THE AUTHOR'S SUMMARY.

ON THE SUBJECT OF ORDERLY OR LAWFUL BEHAVIOR. C. ANDERSON ALDRICH, Pediatrics **1**:725 (June) 1948.

Many physicians interested in modifying the rules of child management to conform to the normal development of children are disturbed by the fact that their efforts are misunderstood and thought to be neglectful of obedience and discipline.

This paper considers, first, the social situation that exists today as a setting for bringing up children; second, the laws for behavior as we find them at present; third, the methods available for controlling behavior, and, fourth, what changes can be made in our codes to obtain more orderly and lawful behavior in young children.

The following points are noted:

1. The environment today is intensely disorganized and ill adapted to good child care.

2. Every child is influenced by two sets of codes for behavior; the first one, set up by his own civilized environment, is recent in origin and is aimed at adjustment to civilized living. It is extremely variable and is imposed from without. The second, which is ordained by his own developmental forces, is ancient, protective, uniform and inherent. Since these two codes often oppose each other, the child is in difficulty from the start, and confusion and poor behavior result. The problem resolves itself into how to influence children to control developmental urges enough to conform, or how to modify social laws to adjust to the nature of growth.

3. The methods of obtaining conformity are those that are persuasive or nonpunitive and those that imply corporal punishment. Neither system is perfect as employed today.

It is concluded that, so far as early childhood is concerned, lawful behavior is much easier to secure when the civilized codes can be adjusted to fit the realities of growth. These adjustments include such practical matters as when to fondle newly born babies, the adoption of a self-regulating feeding schedule, the delaying of toilet training until the child matures enough to cooperate, adjustment of sleep habits; in short, the recognition in rules for behavior of definite maturation points in a child's development which need to be respected.

FROM THE AUTHOR'S SUMMARY.

THE PSYCHOTHERAPEUTIC ROLE OF THE PEDIATRICIAN. MILTON J. E. SENN, Pediatrics **2**:147 (Aug.) 1948.

The pediatrician recognizes his opportunities in mental hygiene and preventive psychiatry and is concerned with his role as psychotherapist in his everyday practice with children and parents. Many different technics and methods have been advocated by psychologists, psychiatrists and educators for use of the pediatrician in the areas of psychologic medicine. On appraisal of these impersonal factors, the conclusion is reached that the essential ingredient of successful psychotherapy consists of a process which allows an interplay of personal feelings between physician and patient. In this paper the psychologic and social roles of pediatrician and patient are evaluated. The author is of the opinion that it is imperative for every physician to understand himself as a person, as well as the patient as a person, in order that he may participate objectively and therapeutically in the physician-patient relationship. Inasmuch as there is a similarity between this relationship and the teacher-pupil relationship, it is suggested that physicians in training have ample opportunity for relating themselves emotionally with their teachers, so that they may obtain psychologic insight, along with medical understanding, in the fundamentals of child care.

FROM THE AUTHOR'S SUMMARY.

PARANATAL FACTORS AFFECTING ADJUSTMENT IN CHILDHOOD. STUART SHELTON STEVENSON, Pediatrics **2**:154 (Aug.) 1948.

In an attempt to determine those paranatal factors which may affect adjustment in childhood, 226 children were studied. These children were followed in connection with a longitudinal study of child health and development; accurate, extensive data were available concerning their mothers' obstetric histories, their neonatal periods and their mental and emotional makeups.

Their general physical conditions during the first two days of life were evaluated as "good" or "poor." These ratings were made without reference to other than neonatal data. Their general adjustments to their environments up through at least 5 years of age were also rated independently, judged by the progress notes of psychologists, pediatricians, social workers and nurses and by parents' comments concerning the children. Data concerning the child's gestation, birth, neonatal period, intelligence and family situation were then studied.

Table 1 shows a highly significant relationship between childhood maladjustment and poor physical condition in the first days of life. When such factors as toxemia, primiparity, long labor, abnormal delivery, prematurity, twinning, cyanosis during the first twelve hours of life, need of resuscitation or an appreciable interval between birth and establishment of respiration are tabulated, it is found that each of these factors results in an increased incidence of children who are in poor physical condition in their neonatal periods. However, the relationships shown in the table are maintained to varying degrees in the presence of each of these factors. This suggests that any of the factors may be responsible in part for the physical condition of the newborn infant, but that no one of them alone is critically causative of childhood maladjustment.

First-born children and only children show a greater incidence of maladjustment following good physical condition in the first days of life, as is to be expected. However, even within these two groups of children, the relationships shown in the table are maintained.

The percentage of children in good physical condition in the neonatal period decreases slightly as the intelligence quotient decreases, but again the relationships of the table are maintained at different levels of intelligence.

Among the 226 children were 92 siblings in forty-one families. There was no consistency of neonatal condition or childhood maladjustment within a given family group. This suggests that environment was not a major factor in determining the adequacy of their adjustment.

It may be concluded that the child's physical condition during his first days of life may affect his adjustment in later childhood and that several paranatal factors may incluence this physical condition. It is to be hoped that these factors may be studied with a broader perspective for their possible effects beyond the first days of life.

FROM THE AUTHOR'S SUMMARY.

PSYCHOTHERAPEUTIC ASPECTS OF PEDIATRIC PRACTICE. HILDE BRUCH and DONOVAN J. MCCUNE, Pediatrics **2**:405 (Oct.) 1948.

Attention is drawn to the psychotherapeutic possibilities inherent in the practice of pediatrics. There is increasing awareness of the need for more attention to the emotional problems of childhood, which has been accompanied with a certain uneasiness about the dangers and difficulties involved. Such objections might be justified if one considers as the approach to psychologic problems only the special psychotherapeutic technics which have been evolved for the treatment of neuroses and psychoses.

The doctor-patient relationship (in pediatrics frequently a doctor-mother of patient relationship) carries within itself psychotherapeutic possibilities fundamentally the same as those which operate in the most intricate psychotherapeutic situation. Application of modern psychiatric knowledge to pediatric practice has usually been in the direction of outlining specific methods of child rearing, such as advocation of self-demand feeding as opposed to scheduled feeding. The possibilities of an individualized utilization of the interpersonal situation usually has been overlooked. This aspect is illustrated by case histories showing the danger of indiscriminate use of "modern" psychology in the care of infants and children and the need for a more individualized approach. Other examples include the psychologic problems of the medical management of chronically sick and handicapped children.

FROM THE AUTHORS' SUMMARY.

Diseases of the Ductless Glands; Endocrinology

HYPOGENITALISM DURING THE USUAL TIME OF PUBERTY. LEWIS M. HURXTHAL, J. A. M. A. **136**:12 (Jan.) 1948.

Hypogenitalism at puberty is defined. A prepubescent testicular volume of 2 cc. (1.7 by 0.8 cm.) is considered normal. Fröhlich's syndrome (adiposogenital dystrophy) and Levi-Lorain (hypophysial) infantilism mean dwarfism, as well as retarded sexual development. The usual tall fat boy has normal genitalia hidden in fat.

The various types of hypogenitalism at puberty are discussed, including diagnosis, treatment and prognosis. Use of urinary gonadotropins and bone age studies are usually of little value. The consistency, as well as the size, of the testes is a helpful sign—the soft testes indicate need for treatment.

A testicular biopsy specimen taken at the age of 14 or 15 years may show (1) immature testes connoting good prognosis with or without treatment, (2) variable degrees of sclerosis and (3) varying degrees of genital development, perhaps with complete lack of spermatogonia.

Without biopsy, treatment is divided into three courses: (1) watchful waiting until 15 to 16 years, (2) administration of chorionic gonadotropin in doses of

500 to 1,000 units three times each week for two months or (3) administration of testosterone, 20 to 30 mg. a day by mouth. The author is opposed to heavy dosage with testosterone because it inhibits pituitary action. In some cases testosterone may have to be given indefinitely.

KIMBALL, Evanston, Ill.

LINGUAL GOITER. EMIL GOETSCH, Ann. Surg. **127**:291 (Feb.) 1948.

The favored site for the occurrence of thyroid tissue in the tongue is at its pharyngeal portion in the region of the foramen caecum. The term lingual thyroid is correctly used when there is a thyroid gland in the neck and when the lingual tissue functions as an accessory thyroid gland. The term lingual goiter should be applied to the presence of hypertrophic thyroid tissue at the base of the tongue in those instances of nonmigration of the thyroid anlage from the region of the foramen caecum.

Lingual thyroid nodules have been described as being as large as an orange or as small as a pea. The surface is usually smooth. The color is dusky, purple, reddish brown or blue. It seems that two thirds to three fourths of the symptom-producing lingual nodules at the base of the tongue may be without a thyroid gland in the normal location.

At least 90 per cent of the patients with a lingual thyroid nodule have symptoms of pressure and obstruction, such as dysphagia, dysphonia and dyspnea. It appears that lingual goiter has never been successfully treated by medical measures. In 1 reported case, strong iodine (Lugol's) solution produced a considerable diminution in the size of the tumor.

Since the outstanding symptoms of lingual goiter are usually the result of some degree of pharyngeal and laryngeal obstruction, treatment is surgical. The most disturbing and also the most commonly expected complication of the surgical treatment is thyroid insufficiency. This is adequately controlled by the administration of small doses of thyroid extract.

The author reports 3 cases.

BANTIN, Omaha.

THE RESISTANCE OF THE YOUNG RABBIT TO THE DIABETOGENIC EFFECT OF ALLOXAN. CARL SWAN SHULTZ and JAMES R. DUKE, Bull. Johns Hopkins Hosp. **82**:20 (Jan.) 1948.

Most of the studies on alloxan diabetes were on adult animals, but one study showed that the fetal rabbit is not susceptible to alloxan.

The authors reported that rabbits given an injection of 300 mg. of alloxan per kilogram of body weight (a dose 50 per cent greater than that which produces diabetes in the adult animal) before the ninth day of life failed to show diabetes. In 4 of these animals an injection of 200 mg. per kilogram of body weight at 1 to 6½ months of age produced diabetes.

There are an excellent theoretic discussion, a bibliography and nine photomicrographs.

LYTTLE, Los Angeles.

CONCERNING THE MECHANISM OF DIESTRUM DURING LACTATION IN THE ALBINO RAT. L. DESCLIN, Endocrinology **40**:14 (Jan.) 1947.

Histologic changes in the pituitary during lactation were mentioned in the rat as early as 1932 by Haterius, who attributed them to the influence of the persisting corpora lutea of lactation. In the author's opinion, this concept cannot be maintained, in view of his later results which demonstrated that the changes of the pituitary during lactation persist after castration in the rat, provided suckling is allowed.

In this paper he extends his earlier researches and shows that in spayed postpartum rats whose main milk ducts had been cut, the mere stimulation of the nipples by suckling prevented the appearance of castration cells in the pituitary. The injection of prolactin in spayed normal or in spayed postpartum animals whose young had been removed did not prevent the appearance of castration cells in the anterior lobe of the pituitary gland.

JACOBSEN, Buffalo.

MENTAL DISORDERS IN CHILDHOOD DUE TO ENDOCRINE DISORDERS. M. SYDNEY MARGOLESE, Nervous Child **7**:55 (Jan.) 1948.

This is an excellent article because of the clear, concise manner in which it (1) describes the action and interaction of the endocrine glands; (2) indicates the relationship of the endocrine glands and autonomic nervous system to the higher brain centers, (3) describes the pathologic conditions resulting from hypofunction and hyperfunction of the glands of internal secretion and glandular unbalance, and (4) describes the relationship between glandular disorders and pathopsychologic states in childhood.

The article is a summary of present day opinion and knowledge.

BEVERLY, Oak Park, Ill.

EPIDEMIC CEREBROSPINAL MENINGITIS (WATERHOUSE-FRIDERICHSEN SYNDROME) IN RELATION TO SULFAPYRIDINE THERAPY. IGNAZIO TRAINA, Pediatria **55**:1 (Jan.-March) 1947.

After examining the literature on epidemic cerebrospinal meningitis (Waterhouse-Friderichsen syndrome) which is already considered a nosologic entity, the author comes to the conclusion that nearly all cases are of the acute meningococcic form in subjects with a decided sensitivity toward such a germ, perhaps because of their particular constitutional state (thymus lymphaticus?).

He reports on 2 patients who recovered after being treated with sulfapyridine at the beginning of the disease. The diagnosis was verified from cultures of the spinal fluid in the first patient and from a hemorrhagic cutaneous spot in the second. The fatal prognosis was modified by the use of sulfapyridine, whose immediate effect on meningococcus is universally known. It is possible that penicillin or the antiserums may give more successful results, but the general use of these new methods in medical practice is still distant. Each physician should then feel it his duty to prescribe without loss of time large doses of sulfapyridine, if possible, intravenously, for all those patients in whom a particularly severe development of an acute febrile condition makes one suspect beginning meningococcic sepsis.

FROM THE AUTHOR'S ABSTRACT.

PATHOGENESIS OF SO-CALLED THYMIC DEATH. MARCELLO BOLLETTI, Riv. di clin. pediat. **44**:730 (Dec.) 1946.

After a brief review of the clinical and anatomic aspects and pathogenetic theories concerning sudden death in general and thymic death in particular, the author describes 4 cases of sudden death of children who had no anatomic evidence of thymic hypertrophy; 3 of the reports included anatomic and histologic studies.

From facts brought out by the cases described and from the copious literature, the author concludes that all sudden deaths—*sine materia*—are of cardiac origin produced by constitutional vagal hypertonia. For the term thymic death must be substituted vagal death.

FROM THE AUTHOR'S ABSTRACT.

HYPOPHYSIAL DWARFISM. G. J. UBBINK, Maandschr. v. kindergeneesk. **16**:394, 1948.

It is still difficult to make the diagnosis of hypophysial dwarfism. In 2 patients, 7½ and 4 years of age, Ubbink based the diagnosis of hypophysial dwarfism on the clinical picture, after excluding the other causes of dwarfism.

In the first patient the therapy consisted of methyltestosterone U. S. P., 10 mg. daily, or a total of 3,800 mg.; during the first month and the last three months of treatment the patient also received 5 × 50 mg. of thyroid. In fourteen months the height of the boy increased 13 cm., while the testes, which at the beginning of the treatment could not be palpated, descended totally.

The other patient was given injections of chorionic gonadotropin (pregnyl®), a total of 14,400 units in the course of four months, with an interval of two months after the first month of treatment. The result was nil; only the testes descended. Changes in the epiphysis, which might indicate an early closure as the result of the therapy applied, could not be observed.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Muscles, Bones, Joints and Lymph Glands

OSTEOMYELITIS OF THE FACE AND SKULL. HANS BRUNNER, Illinois M. J. **93**:213 (April) 1948.

In this paper an attempt is made to classify 22 cases of osteomyelitis of the skull and face according to the causes of the disease. The author classifies them as metastatic osteomyelitis, traumatic osteomyelitis, osteomyelitis in chronic frontal sinusitis, osteomyelitis in acute frontal sinusitis and postoperative osteomyelitis. Case reports and a general discussion are included in the article.

O. BARBOUR, Peoria, Ill.

INFANTILE CORTICAL HYPEROSTOSES. AMOS C. GIPSON and BENJAMIN J. CLARK, Pediatrics **1**:221 (Feb.) 1948.

A new syndrome called infantile cortical hyperostoses was described by Caffey in 1939. It is characterized by (1) tender swelling deep in the soft tissues, (2) cortical thickenings in the skeleton and (3) onset during the first three months of life.

In the case presented, swelling and tenderness developed over the right forearm before the age of 2 months. Later, swelling and tenderness developed successively in the mandible, clavicles, several ribs and one scapula. The swellings were deep and firm. They showed no pitting on pressure and no unusual warmth or discoloration. The swelling of the soft tissues was confined to the areas of the hyperostoses, but there were small hyperostoses visualized roentgenographically in several bones where soft tissue swellings were absent. In all the skeletal lesions the findings were the same: cortical hyperplasia under a proliferating periosteum. Recovery from the fever, tenderness and soft tissue swelling occurred in this case after several weeks; but the hyperostoses remained unchanged roentgenographically.

FROM THE AUTHORS' SUMMARY.

MYASTHENIA GRAVIS IN YOUNG CHILDREN: REPORT OF THREE CASES—ONE CONGENITAL. J. ROBERT BOWMAN, Pediatrics **1**:472 (April) 1948.

There are reports of 14 cases of myasthenia gravis occurring in children under 10 years of age. During the past three years, 3 children, aged 3 7/12, 4 9/12 and 8 3/12 years, with myasthenia gravis have been treated at the Children's Hospital, Boston.

These patients were reported on because of the rarity of the disease in children so young, and particularly since myasthenic symptoms and signs were evident in 1 child at birth. This child, a 3 7/12 year old boy, was observed to have drooping eyelids and a weak voice at birth. Dysphagia followed a severe attack of bronchopneumonia at the age of 13 months. More or less generalized muscle weakness and increased fatigability gradually developed. This child, as well as the other 2 children, showed the typical myasthenic response to a test with neostigmine methylsulfate (prostigmin®) and improved rapidly when treated with neostigmine bromide. Photographs before and after the "prostigmin® test" are included. All children having ptosis of the eyelids should be given the "prostigmin® test." The first case of the series was the first of congenital myasthenia gravis to be reported.

FROM THE AUTHOR'S SUMMARY.

ACUTE HEMATOGENOUS OSTEOMYELITIS. EDWARD B. SELF, Pediatrics **1**:617 (May) 1948.

One hundred and thirty-eight children with acute osteomyelitis admitted to Babies Hospital, New York, between 1930 and 1946 are the subject of this report. An unexpected number of cases resulted from infection by hemolytic streptococci. The behavior of hemolytic Staphylococcus aureus is compared with that of hemolytic streptococci in osteomyelitis. Mortality was greatest with extreme youth, chronicity least with youth.

Administration of massive doses of penicillin in the earliest stages of the disease constitutes the treatment of choice, and emphasis should be on the "treatment of the child," rather than on treatment of the bone. Surgical intervention should be postponed in the early stages and used later only to drain abscesses of the soft parts or abscesses of the bone which are well localized and not regressing.

The treatment of chronic osteomyelitis is an entirely different problem. Radical removal of diseased bone and sinuses, with primary closure of the wound, is the treatment of choice. Immobilization, treatment with penicillin and obliteration of dead spaces by the use of muscle and skin grafts are important adjuncts to success.

FROM THE AUTHOR'S SUMMARY.

FRACTURE OF THE ANTERIOR SPINE OF THE ILIUM: REPORT OF FOUR CASES AND DISCUSSION OF TREATMENT. J. ROSWELL GALLAGHER, Pediatrics **2**:186 (Aug.) 1948.

Four case reports of fracture of the anterior spine of the ilium emphasize the symptoms which characterize this injury and the effect of brief conservative treatment. This fracture should be suspected when sudden severe pain develops in the inguinal region during the course of some strenuous exertion or athletic activity; its occurrence during short foot races has led to the name "sprinter's fracture." The initial pain is severe, and there may be vomiting; raising of the extended leg is impossible, and there is tenderness over the injured area. When these signs and symptoms are present, a roentgenogram should be taken to distinguish a fracture of an anterior iliac spine from such conditions as a tear of the quadriceps muscle. Some of these injuries can be prevented if athletes are compelled to "warm up" prior to making those maximum efforts which put severe strain on the points of origin of the large muscles of the thigh. In none of these cases was surgical intervention observed to be necessary. In each instance complete recovery followed a short period of rest in bed with the knee flexed. A period of two to three weeks of rest in bed with knee flexed, following which activity was gradually increased, was found as effective as, and more efficient than, nailing the fragment, applying a plaster spica or six weeks' rest in bed.

FROM THE AUTHOR'S SUMMARY.

SKELETAL GROWTH IN PYRIDOXINE DEFICIENT MICE. RUTH SILBERBERG and BARNET M. LEVY, Proc. Soc. Exper. Biol. & Med. **67**:259 (March) 1948.

A study was made of 28 mice, half of which were given a diet lacking pyridoxine and the other half a diet complete except for pyridoxine but which contained 54 per cent casein. In these pyridoxine-deficient young mice, the growth of cartilage and formation of bone were inhibited and finally ceased. On refeeding the complete diet, recovery was noticeable after three days and was still in progress after fourteen days. The growth processes were quickly restored, with mitoses present in the germinal layer of the cartilage, as well as in the osetoblasts.

The effects of pyridoxine deficiency on the cartilage resemble those seen in mice deficient in pantothenic acid, and the disturbance of ossification was not unlike that observed in riboflavin deficiency. It may be that this difference indicates a specific effect of the pyridoxine deficiency; however, it might well be a manifestation of the more pronounced sensitivity of mice to the deficiency as compared with rats. The feeding of a high protein diet accentuated the effects of pyridoxine deficiency, inasmuch as growth of cartilage and bone was more inhibited than in the pyridoxine-deficient mice receiving a diet with the usual casein content.

HANSEN, Galveston, Texas.

TREATMENT OF FRAGILITAS OSSIUM. S. VAN CREVELD, P. ARONS and E. VAN WYK, Maandschr. v. kindergeneesk. **16**:253, 1948.

Of late, various therapeutic measures have been recommended for the treatment of fragilitas ossium. Glanzmann gave his patients large doses of vitamin D; but in applying this therapy one has to be careful to avoid deposition of calcium in other organs. Ropes, Rossmeisel and Bauer considered fragilitas ossium to be a disturbance in the osteoid tissue, and, therefore, they recommended a treatment with estrogenic substances. The effect of this therapy was greater in boys than in girls. Reifenstein and Albright looked on this disease as a result of deficiency of protoplasm in the bone matrix, and they, therefore, prescribed a diet rich in protein.

The authors applied these therapeutic regimens in 3 patients: 2 boys, 3½ months of age, and a girl, 6 months old, all with fragilitas ossium (Vrolik). Under the influence of several courses of treatment with estradiol U. S. P. (dimenformon®), 8 × 1 mg. until cure, the calcium balance in the boys became more positive; the nitrogen balance decreased in one of the boys and remained the same in the other. In the girl, who received slightly larger doses, it was impossible to perform balance studies on account of technical difficulties. During this treatment with estrogenic substances all 3 patients acquired new fractures.

Directly after the treatment with estradiol, the boys received in the course of fourteen weeks 2,400,000 units of vitamin D_3 intramuscularly, and the girl, who had already been given several shock doses of vitamin D, received in the course of six weeks 1,200,000 units of vitamin D_3 intramuscularly. After this, the boys showed no new fractures, the girl only one.

The values for calcium, phosphorus and phosphatase in the boys were normal and remained so. The girl showed a transitory slight diminution of the values of calcium and phosphatase. The phosphorus content was low and remained at that level.

The girl had two further treatments, lasting nine and eight days, respectively, with 200 cc. of cow's serum given orally daily. It was tolerated well, but the total protein content of the blood decreased, especially because of a diminution in

the globulin content. After the last treatment, the girl still had one new fracture. The general condition of these 3 children clearly improved under the influence of the various treatments, but roentgenologically, no changes occurred.

VAN CREVELD, Amsterdam, Netherlands.

EOSINOPHILIC GRANULOMA. BERNHARD BESKOW, Nord. med. (Hygiea) **30**:965 (April 26) 1946.

A boy 8 years of age displayed fatigue, anorexia, emaciation and purpuric cutaneous manifestations. He was first examined two months later. There were, in addition to the purpuric spots, a lymphoma of the neck, an enlargement of the axillary and the inguinal glands, moderate hepatomegaly, no splenomegaly, anemia of the sideropenic type, normal thrombocytes, clotting time, capillary fragility and bleeding time, increased sedimentation rate and enlargement of the hilus of the right lung. At the distal part of the left femur a decalcified focus of cherry size was noted. Eosinophilia of the blood was 27 per cent, with abundant eosinophils in the bone marrow and lymphatic glands. During the following one and one-half year these morbid symptoms gradually disappeared, and he was at last considered healthy.

WALLGREN, Stockholm, Sweden.

OSTEOPETROSIS (MARBLE BONES). IB SÖNDERGAARD, Nord. med. (Hospitalstid.) **32**:2843 (Dec. 13) 1946.

Two sisters, 1 and 3 years old, had osteopetrosis (Albers-Schönberg disease). In the older cranial decompression was carried out, without any evident amelioration of the condition. This child died six months later. In the younger child suboccipital decompression was performed with good effect on the intracranial hypertension.

WALLGREN, Stockholm, Sweden.

Diseases of the Eye

A REVIEW OF COMMON OCULAR PROBLEMS IN CHILDREN. MARTIN K. KOKE, California Med. **68**:370 (May) 1948.

In a review of the case records of 1,941 children, it was found that 1,244 refractions were done. The ordinary ocular complaints which lead the parents or the physician to suspect the need of glasses are listed. The only two complaints which indicated the need of glasses in the majority of children were poor vision and strabismus. The other complaints in the vast majority of the series were not attributable to refractive errors.

Concomitant squint was present in 224 children. Of these, 177 had a refractive error that was at least partially responsible for the squint, and glasses were prescribed. All children who have squint or who are suspected of having it should have a refraction done after use of a cycloplegic drug. The dominant nonsquinting eye in children with monocular squints should be occluded as early as possible. Surgical operation and orthoptics should be used to restore the proper alinement and fusion. The commonest external diseases are blepharitis, conjunctivitis and occluded nasolacrimal ducts. A few suggestions for their management are made.

There were 69 children with intraocular disease, with 22 different causative entities. Congenital cataract was the commonest. Developmental anomalies or congenital diseases were present in 39 children. Trauma accounted for most of the remainder.

Of 2,432 ocular problems, 1,244, or 51 per cent, were caused by refractional abnormalities; 258, or 11 per cent, were the result of abnormalities of the extraocular muscles; 861, or 35 per cent, were due to external diseases, and 69, or 3 per cent, were caused by intraocular maladies.

PRYOR, Redwood City, Calif.

VERTICAL DEVIATIONS. J. MCGILLIVRAY, Canad. M. A. J. **58**:361 (April) 1948.

Early treatment of vertical deviations, as is practiced in lateral squints, is urged. Refractions should be done early and occlusion of the weaker eye instituted. Orthoptics may be instituted later. The aim is to prevent the development of false or true amblyopia. In operative corrections, the inferior oblique muscle is recommended as the site of choice.

MCGUIGAN, Evanston, Ill.

CORNEA VERTICILLATA. M. GRUBER, Ophthalmologica **112**:88 (Aug.) 1946.

In a previous article (*Ophthalmologica* **111**:120, 1946) the author had reported cases of this rare corneal disease. In the second article, he describes additional cases of cornea verticillata in a second family. He is of the opinion that it is an unusual hereditary variation of physiologic character, but the manner of transmission is not as yet completely known. Good illustrations of the condition are given in the paper.

F. H. ADLER [ARCH. OPHTH.].

TWO CASES OF ABLATIO RETINAE CONGENITA NONFALCIFORMIS. H. MOLLER, Acta ophth. **23**:353, 1945.

Bilateral detachments of the retina were observed in a boy of 5 years. No tears or other changes were found. One eye was removed because the presence of a malignant growth was suspected. None was found. Later examination of a younger brother, aged 2, showed a similar condition in one eye.

O. P. PERKINS [ARCH. OPHTH.].

Skin Diseases; Allergy

RESPIRATORY MOLD ALLERGY: A TWELVE MONTHS' ATMOSPHERIC SURVEY IN SAN FRANCISCO. WILLIAM C. DEAMER and HERBERT W. GRAHAM, California Med. **66**:289 (May) 1947.

A report is made on the type and frequency of mold spores detected over a one year period in the atmosphere of San Francisco.

Alternaria spores were shown to be relatively absent, while Hormodendrum was the commonest spore observed. These two molds are probably of chief clinical importance in other sections of the United States.

No striking seasonal incidence of mold spores was observed. This makes recognition of the patient with respiratory complaints due to mold sensitivity more difficult than it would be if a clearcut seasonal incidence were present.

PRYOR, Redwood City, Calif.

THE PRESENT-DAY TREATMENT OF ASTHMA. M. COLEMAN HARRIS, California Med. **66**:354 (June) 1947.

The specific treatment of bronchial asthma consists of eradication of the cause, allergic or infectious, or both, as the case may be. When eradication is impossible or inadvisable, separation of the patient from the specific allergic causes, or immunization to them, is indicated. To arrive at the primary cause of bronchial

asthma requires a careful and complete investigation, using not only cutaneous tests, valuable as they are, but also keen perceptive powers and a scrutinizing physical examination which must be complete and thorough. This point is stressed most strongly.

The psychologic effects of bronchial asthma should not be ignored but instead studied and corrected in order to decrease the severity and frequency of attacks.

For acute attacks of asthma nothing surpasses epinephrine, in dilution of 1 to 1,000, subcutaneously. In prolonged attacks epinephrine may be repeated, and in addition, such drugs as aminophylline intravenously or rectally, helium and oxygen by inhalation and 50 cc. of 50 per cent glucose solution intravenously are helpful. The inhalation of epinephrine, in dilution of 1:100, is of inestimable value in many cases, for it may give almost immediate relief, while orally ephedrine sulfate is still useful in preventing attacks. Epinephrine in oil administered intramuscularly prolongs the action of the drug. Potassium iodide is still helpful in liquefying tenacious mucous plugs. Instillations of iodized oil should be employed only as a last resort.

The popular antihistaminic agents, diphenhydramine (benadryl®), hydrochloride and tripelennamine (pyribenzamine®) hydrochloride, should be used with caution. In bronchial asthma, especially the perennial type, they do not appear to be as valuable as in other allergic conditions. The side effects are disturbing and limit their use.

PRYOR, Redwood City, Calif.

THE EARLY RECOGNITION OF ALLERGIC TENDENCIES IN INFANCY. W. AMBROSE MCGEE, South. M. J. **40**:515 (June) 1947.

The results are presented of a study on 150 well babies under 1 year of age regarding unusual or abnormal signs and symptoms which followed the ingestion of a new food or vitamin preparation. The foods which caused symptoms, in order of their frequency, were orange juice, cow's milk casein, spinach, ascorbic acid, mixed cereals, prunes, tomatoes, cod liver oil, carrots, oats and wheat. The symptoms produced were, in order of frequency, colic, loose stools, eczema, excessive regurgitation, papular rash, constipation, mucus in stools, vomiting, anal excoriation and abdominal pain.

Foods that were disliked did not seem to parallel foods which disagreed, but the author suggests avoiding such foods. Foods which previously have disagreed should be given another trial after they have been avoided for a few months.

LOGAN, Rochester, Minn.

EHLERS-DANLOS SYNDROME: MASKED FORMS AND HEREDITARY CHARACTERISTICS. M. JEUNE, J. ROUX and J. MARTIN, Arch. franç. de pédiat. **3**:547, 1946.

The authors report 6 cases of this curious condition, heretofore sparingly mentioned in the literature. They conclude that the disorder is familial and hereditary, not concerned with syphilitic infection and frequently appearing in a mild form that is easily overlooked. They further assert that the disease is a dystrophy of dominant character transmitted by mendelian law to half the descendants.

AMESSE, Denver.

OCULONASAL TYPE OF JUVENILE ERYTHREDEMA POLYNEUROPATHY. G. CHARLOUX, Arch. franç. de pédiat. **3**:556, 1946.

Among the profusion of symptoms observed in erythredema polyneuropathy of young subjects, those associated with the oculonasal region form a classic variety. While the ophthalmic phenomena are usually grouped under the general title of

conjunctivitis, with photophobia and profuse lacrimation, the author attempts to show in a carefully documented observation that the latter symptoms have their origin in the sympathetic nervous system rather than in the ocular apparatus itself.

The case reported concerns a girl 15 years of age admitted to the division of ophthalmology of the Geneva Hospital, Geneva, Switzerland, for relief of persistent photophobia and lacrimation, accompanied with tachycardia and progressive emaciation. She had been under treatment for hay fever and later for toxic diffuse goiter (Basedow's disease). The diagnosis of erythredema polyneuropathy was made in view of these observations, in addition to increased vascular tension, profuse sweating and the classic picture of cold, swollen extremities. The use of agents such as acetylcholine chloride ameliorated the patient's condition, and complete recovery was reported in seven months.

AMESSE, Denver.

ATTEMPTS AT PROPHYLAXIS AGAINST SERUM SICKNESS. GINO CARDINI, Riv. di clin. pediat. **44**:746 (Dec.) 1946.

The author describes the good results obtained in the prevention of serum sickness with the use of serum taken from patients convalescent from this illness. The illness was prevented in 79.3 per cent of the patients treated. Only 3.4 per cent of the controls were immune.

The author, after examining the various theories on the pathogenesis of this illness, interprets the results obtained through the immunobiologic theory.

FROM THE AUTHOR'S ABSTRACT.

ACRODYNIA. J. P. GARRAHAN and R. R. L. SAMPAYO, Arch. argent. de pediat. **26**:235 (Oct.) 1946.

This is the first part of the paper. It is a review of the literature on the subject and includes discussion on the following points: the definition as given by Rocaz and Péhu and Boucomont; historical aspects; etiologic factors as considered in the literature, such as diseases of the central nervous system (poliomyelitis, encephalitis, Morvan's chorea and miliary fever), deficiency diseases, intoxications and allergy, together with the gastroenteral and infectious theories, and the pathogenesis of acrodynia.

ROJAS, Boston.

Teeth and Dentistry

ORAL HEALTH SERVICES DURING THE PERIOD OF THE PRIMARY DENTITION. KENNETH A. EASLICK, J. Dentist. Child. **15**:3, 1948.

In view of the low income level of the younger instructors at Ann Arbor, Mich., and their inability to buy preventive pedodontic materials, a survey of the opinions of nineteen teachers was made to determine what constitutes adequate dental care to maintain good health in children.

The twenty-two services listed read much like "what every young dental graduate should know." They are so fundamental that one wonders why the nineteen teachers would not be in full accord. A diversified reaction to the problem of exposed pulp can be understood. No mention was made of the systemic health of the child in consideration of risk. The five choices of treatment for an exposure of vital pulp were determined by the experience of the operator.

Sixteen of the teachers were in full accord with the use of space maintainers; fourteen approved of a biannual prophylaxis; fifteen approved of the use of bite-wing roentgenograms; thirteen approved of the utilization of counts of oral Lactobacillus acidophilus for checking the dietary control of rampant caries.

Fifteen approved of filling the cavities in both posterior and anterior teeth with silver amalgam.

The survey resulted in no conclusion concerning what could be eliminated from the list of "essential" services. It is impossible to discuss such an important question in a brief outline form. The wide variation of opinion might be indicative of a need for further study.

WHITFIELD, Evanston, Ill.

INFLUENCE OF FLUORINE IN MOTTLED TEETH ON DENTAL CARIES. VIRGIL D. CHEYNE, Proc. Soc. Exper. Biol. & Med. **67**:149 (Feb.) 1948.

For this study there were selected a total of 18 rats from three mothers which had been receiving daily concentrations of 300 to 350 parts per million of fluorine as potassium fluoride during pregnancy and a total of 27 young from five mothers which received no fluorine. One half of the fluorinized young and 12 of the 27 nonfluorinized young were subjected to total extirpation of the salivary glands at the age of 24 days. At 42 days the animals were placed on a caries-producing diet and were studied after being on this diet for one hundred and four days. It was observed that the reduction of saliva greatly increased the incidence of caries in the rat. Normal animals on the caries-producing diet averaged 4 carious cuspal involvements and 1.8 carious teeth per animal; those with salivary glands extirpated averaged 36.6 carious cuspal involvements and 10.6 carious teeth per animal; those with mottled molars averaged 5.4 carious cuspal involvements and 1.5 carious teeth per animal, and desalivated rats with mottled molars averaged 28.1 carious cuspal involvements and 8.5 carious teeth per animal. The number of cavities in the lower teeth exceeded those in the upper for all animals examined. Because the average number of carious teeth in the third group is only slightly lower than normal, it seems that the fluorine incorporated in the substance of the tooth had little, if any, influence in retarding caries. The greater number of carious cuspal involvements in the same group gives added support to this assumption. The outstanding conclusions, however, are based on the comparison of the last group with the remaining three. Desalivated animals with mottled molars showed an increase of approximately 80 per cent of carious lesions over normal animals and only about 20 per cent reduction compared with desalivated animals not subjected to treatment with fluorine in their prenatal period. There is evidence that saliva offers greater protection than fluorine in the substance of the tooth.

HANSEN, Galveston, Texas.

Miscellaneous

CHARCOT-LEYDEN CRYSTALS: A STUDY OF THE CONDITIONS NECESSARY FOR THEIR FORMATION. MAX SAMTER, J. Allergy **18**:221 (July) 1947.

This is a report of a series of interesting experiments conducted in the endeavor to learn something of the formation of Charcot-Leyden crystals. Specimens of blood obtained from patients who had varying absolute eosinophil counts, fluid obtained from blisters of various cutaneous conditions, fluid obtained from blisters produced by the application of cantharides to the skin and smears of nasal secretion from persons with allergic rhinitis were studied. The preparations were observed for fourteen days.

The crystals formed in the eosinophils of the blood. The formation was observed in individual cells, but not all eosinophils produced them. Eosinophils in blister fluid and nasal secretions failed to produce the crystals. It is assumed that two factors are necessary for the formation of the crystals; an endogenous factor consisting of cellular material undergoing autolysis and a contributing exogenous factor.

HOYER, Cincinnati.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

John L. Reichert, M.D., *President*

Oct. 19, 1948

Round Table Discussion on School Health

Henry G. Poncher, M.D., *Moderator*

DR. HENRY G. PONCHER: I shall violate the function usually assigned a moderator and give a prologue that might interest this group.

The material I am presenting is in the report of the Committee for the Study of Child Health Services of the American Academy of Pediatrics (Child Health Services and Pediatric Education, New York, The Commonwealth Fund, 1949, pp. 114-119). The survey made by that body did not attempt to gather data on all aspects of the complete program of health service for school children, nor did it undertake to evaluate the respective merits of medical service provided in schools as contrasted with that provided on referrals of children to private physicians for school health examinations. The school health examination provided at school is the commonest practice and the one that lends itself best to study. The criteria adopted by the committee are admittedly weak, and the results must, therefore, be evaluated from that point. It was decided not to attempt to enumerate something as heterogeneous as a school health examination as variously conceived. The amount of school health service is presented in terms of presence or absence of the service, county by county. Administration and service are often not on a county basis but on a school district or even on individual school basis. The proportion of the child population of a county thus covered is unknown. The smallest population base with which the survey could work on a national basis was the county. The positive statement of the number of counties having school health service was a gross overstatement, since a given county was credited for school health service if such service was present in the public elementary schools. I shall emphasize later the reason that was significant. The negative statement, therefore, of the number of counties that do not have school health service has more meaning, and that is the part I should like to stress—the negative aspect of the report.

For the entire United States, there were 1,545 counties, more than half the counties in the country, which did not have any school health service by the previously stated definition; nearly 5,000,000 children, or 22 per cent of all children from 5 to 14 years of age, lived in such counties. As would be expected, practically no metropolitan counties were without such service, but in isolated rural counties the deficiency rose as high as 61 per cent. Nine hundred and sixty-five counties had neither medical nor nursing service, and that comprised 11 per cent of the entire school-age population. The regional picture for school health service, as for most services, showed the deficiency greatest in the southeastern, the southwestern, the mountain and the plains states. The state range is exceedingly wide; 10 states had 50 per cent or more of their counties uncovered by school health programs.

The administration of school health service is a matter of controversy. There is agreement on some aspects, as, for example, health education is primarily a job for educational authorities and the control of communicable diseases should rest with the health agency. The administrative pattern in operation at local levels was as follows: The official educational agencies took care of 45 per cent, the official health agencies, 41 per cent, joint educational and health agencies, 11 per cent, and other agencies of a voluntary nature, 3 per cent. There was greater tendency for educational authorities to provide health service in metropolitan counties and for health agencies to be responsible for the isolated counties. At present, 69 per cent of the health service in metropolitan counties is provided by educational agencies as against 16 per cent in the isolated counties, and 16 per cent is provided by health agencies in metropolitan counties as contrasted with 71 per cent in isolated counties.

The frequency of health examinations was also studied. The present practices are divided fairly evenly among three patterns: first, examination of pupils once a year; second, examination of those in certain grades once a year, and third, examination on referrals only. Emphasis appears to be given by educational agencies to examination of all children yearly, that is, 64 per cent have that practice, while health agencies appear to be more selective in this respect. Of 8,000 physicians rendering school health service in part or full time capacity, about 20 per cent were health officers. As in the case of the well child conference, the percentage of health officers working in metropolitan counties is small and increases as one goes out from the centers; 3 per cent of metropolitan counties have health officers in the school service as contrasted with 59 per cent in isolated rural areas. The great majority of physicians conducting school health examinations were not health officers; 94 per cent were general practitioners and 4 per cent were pediatricians. The pediatrician plays a much smaller role in school health examinations than in well child conferences, of which more than one fourth of the sessions were conducted by him.

This, in a concise way, is the national picture, and you notice that no analysis was made of the school health program as contrasted with school health examinations, because the sad fact exists that there are few good school health programs in the United States. The bibliography that you were provided with is an excellent blueprint of school health programs which, in fact, do not exist in the majority of enlightened states; so the truth is that, while a great amount of lip service is given to school health programs and examinations, there are few model school health programs in operation.

Having briefly touched on conditions at the national level, I do not have much to contribute from the state level. The analysis of the state of Illinois shows not only that it is sorely lacking in adequately conceived school health programs, but that school health examinations are poorly carried out and that there is much disagreement at present on the way in which school health examinations should be conducted.

In the short discussion that each member of the round table will give, not only do I hope that each will indicate his idea of what would constitute an adequate school health program—and certainly the ones with the major responsibility for that will be Mr. Hunt and Mr. Pritzlaff—but I should like to have the audience contribute to the discussion. I think we should distinguish between a school health program and school health examinations, and I ask Mr. Hunt to give his concept of an adequate school health program, because the others at the round table will be concerned with school health examinations. I should like to ask him how we, as a group of practicing physicians, may fit into such a scheme.

MR. HEROLD C. HUNT (General Superintendent of Schools, Chicago): This is a large order and a challenging one. When I was an undergraduate student at the University of Michigan, I recall in a course on the essentials of teaching exposure for the first time to an interesting and significant document entitled "The Cardinal Principles of Education"—which are seven in number, as some of you may remember. Health was the first, and in discussions in class there was widespread agreement that health was the most important of the cardinal objectives of education, for without health it would be impossible to achieve good citizenship, worthy use of leisure time, worthy home membership, ethical character or any of the other objectives. The seven cardinal principles of education have now been replaced somewhat. In the most recent pronouncement on educational objectives in the United States, for which we are indebted to a group of men and women who are in the vanguard of American educational thought, the Educational Policies Commission, the seven cardinal principles have been reduced to four. First on that list is "self realization"; certainly I need not argue before so interested a group as this that self realization embodies the essentials of health.

This past year I have been chairman of the group producing the yearbook for the American Association of School Administrators, "The Expanding Role of Education." In that book it has been pointed out at some length that health is a basic and major consideration of education within the United States.

The moderator has asked me to indicate my concept of an adequate program of school health. I should like to blueprint that concept in much more detail than will be possible in our limited time. However, I might indicate again by way of emphasis that health is the major objective of education today and that the school program will concern itself with realization of that objective. Its aims will be, then, that boys and girls are equipped properly to come to school; that the technic of the "summer roundup," which has won the acclaim of the nation and in which the Parent-Teachers Association has had nationwide cooperation of physicians, is followed all through the child's school life and that the child comes to school and stays in school, equipped to obtain the fullest benefit from the educational experiences that are to be his. The school program will concern itself with all aspects of health mental, as well as physical, nutritional and dental health, social health and all phases of health adjustment. That is a large order and requires the cooperation of all agencies interested in its fulfilment.

I am delighted to find the cooperative aspects of such an alinement reflected in this symposium. Such a program is not the function of the school system alone. Reduced to its most desirable aspect, the program would come about as a result of intelligent parenthood, the belief in the necessity of equipping children to benefit by educational experience. But we must realize that we live in a community of more than 4,000,000 persons, and that we meet with a variety of parents and a variety of stratums in terms of economic competency. There are others here who are in better position than I to indicate what the economic needs are. Concerned as we are with the educational welfare of almost 400,000 boys and girls in Chicago, we know they come from a variety of homes where there is an interest in equipping the child to benefit by education but by no means the opportunity to realize it. We meet these boys and girls day in and day out, and we, who are mindful of the enhanced conception of the psychologic laws of learning, know that all of a child comes to school, not just his brain. He comes whether or not he has had a good breakfast and regardless of the mental environment of which he has been a part within the last hour or his experiences on the way to school. All this definitely attests to the child's ability to take advantage of the educational process.

I have tried to suggest that the aims and objectives paramount in our educational order, finding reflection in such activity as the summer roundup, might be extended throughout the school program. It is not sufficient to state that summer is the time to do that. There should be—as provided by law in most states and implemented adequately in some states—regularity of examination as these children progress along the educational ladder. Here I should reemphasize the over-all importance of the total health aspect. How is that to be realized? Again I say, by cooperative endeavor. I have long subscribed, and I shall here publicly attest, to the belief that regular examination is best done by the family physician, when there is intelligent interest on the part of the parents and when there are means to make that possible. Where this is not possible, boards of health, departments of health, cooperating agencies, clinics and the like must advance their services to realize the objective.

Here is the place the school comes into the pattern, and here are some of the difficulties that I trust this symposium may help to unravel. I can merely express the interest we, as educators, feel in the problem. I want to indicate the awareness that we share with many of you of the inadequacy of the present system and of our relatively low rank in expenditure per pupil for a health advancement program. Just prior to this meeting, I was furnished by Mrs. John L. Hancock, of the Citizens Schools Committee, with a chart indicating that, so far as ten of the major city school systems of the country are concerned, our relative rank in expenditure per pupil for the years 1946 and 1947 is in ninth position. That is among only the larger city school systems; many smaller school systems lead the way in caring for the health of the child.

Mr. Pritzlaff will go into greater detail on our program, but I want to suggest that we are endeavoring to set up procedures that will realize some of the objectives expressed this evening. Recently, we organized an advisory health council, in which we asked for the participation of the Chicago Medical Society, the Chicago Dental Society, the Department of Health, the Parent-Teachers Association and members of the Board of Education. I merely indicate the formation of this council as what I hope will be recognized as a forward step in the attempt to bring together agencies that should have a vital interest in the problem.

DR. HENRY G. PONCHER: Mr. Pritzlaff, could you give us some idea of the way in which the program outlined by Mr. Hunt can be practically implemented and executed, so far as the Board of Education is concerned?

MR. A. H. PRITZLAFF (Director of Health and Physical Education, Board of Education, Chicago): I shall endeavor to give a picture on the basis of our thinking. We like to think of health in terms of four different phases: The first phase is health service, which, of course, is the work of the physician and the dentist by examination and then follow-up correction of remediable defects, because without such correction the examination is worthless. The second phase is health education, or, if it is classroom instruction, we call it "health instruction." The third phase is healthful school living: the mechanical arrangements about the school, the building itself, the location and the sanitation, in other words, the child's opportunity to live in a healthful environment many hours of the day. Because we are thinking of physical education as well, we like to think that we have health activity in the school program, as good health is an important objective of physical education.

The first two—health service and health education or instruction—overlap quickly, first, because an examination worthy of the name has to be the starting

point of instruction in health. On the other hand, many times our starting point for good practices in health examinations and correction of defects is health instruction. As Mr. Hunt indicated, health service in the Chicago schools is probably inadequate, and we should be the first to admit that. For many years we have endeavored to do something about it but, unfortunately, there has never been provided an adequate citywide program. The Department of Health provides an excellent program of communicable disease control which meets the needs in a definite phase, but by "inadequate" we mean the examination itself and the follow-up work. We have had support of the medical and dental societies in various starts on programs which, unfortunately, never came to anything. Dr. Julius Hess will recall that twenty years ago we were faced with the same problems, probably because Chicago is so large, the conditions so diverse and the funds always inadequate.

In our high schools we devote one period per week in the physical education program to health instruction during all four years. In the elementary schools an excellent program of integrated health education was started many years ago through the efforts of the Elizabeth McCormick Memorial Fund. Unfortunately, that integration seemed to die out. After junior high schools were eliminated, we found that eighth grade children were woefully lacking in health instruction and ability to coordinate what they had received in the lower grades. In a number of elementary schools we started a "health counselor plan." Time was allotted for some health guidance, which included motivating the child to do something about his health needs and to try to interest the parents. In some instances this was successful. A period was also allotted for direct health instruction to children in the upper grades to correlate the work of the previous grades. By motivating the high school students themselves, we were able to have them demand of their parents the opportunity for a health examination. We are trying to do the job for tomorrow and to interest the child so that he will carry on after leaving school. Frequently, he is far ahead of his parents so far as health knowledge is concerned and must carry his parents along with him.

We have been able to obtain excellent results from examinations and correction of defects. A few years ago we started a program to show what might be accomplished with eighth grade graduates preparing for high school in having a medical and dental examination with correction of defects as a starting point. In just two years, approximately 10 per cent of eighth grade graduates consulted the family physician and dentist for examination and correction. However, that does not solve the problem for the remainder. We must remember that in a city of this size we have two extremes; we have those, and there are many, whose parents could do something about examinations and correction of defects, but do not. We also have those at the other extreme, whose parents cannot do anything about it and who must receive help.

In all programs worthy of the name some pattern is followed. This deviates, of course, from a board of education program to a health department program to a cooperative program. Indications are that the last-named pattern seems most desirable; namely, that the boards of health which are conscious of the community, as well as the pupils, have a part in the program. The schools, because of their knowledge of the young people under their control, have a stake in the problem. But it is through the cooperative efforts of all concerned that the sought-for goal will be reached.

There probably never will be sufficient funds in Chicago to take care of examinations and correction of defects for all children. Therefore, a large proportion

must be interested, through education of parents as well as of children, in having the work done through their own channels, leaving the available funds for those unable to care for themselves.

DR. HENRY G. PONCHER: We are sorry that Miss Mary Murphy who has been very active in programs of this kind was unable to attend this meeting because of illness. She has continually stressed the importance of health in any educational venture and not merely as a matter of giving health lessons. Any program with which she has had to do has been valuable, and she has always been able to secure the cooperation of the medical profession in a soundly conceived program and to carry out her objective in most instances.

Dr. Bundesen, will you describe the present service rendered by the Department of Health, and what your concept is concerning participation of the department in a school health program?

DR. HERMAN BUNDESEN (President, Department of Health, Chicago): In the schools, the Health Department in recent years has been and is now placing its entire attention on control of communicable diseases. Such activities include examinations of children who have been absent from school for any cause for forty-eight hours or longer or who return after an illness of any duration. There have been immunologic investigation of individual cases and outbreaks of communicable diseases in the schools, application of measures for their control, inoculations against diphtheria, vaccination against smallpox for children who have not had such by their own physicians and examinations by means of the Wood light for evidence of tinea capitis.

Mr. Hunt is doing a good job as superintendent of schools. He said, in essence, that there is nothing of greater importance to the individual person, the child and the adult, than health. He realizes, as do we all, that on health depends the person's attitude toward life, his whole relationship toward life. By school health we mean the health of the individual children who make up that school. The only organized health program from outside sources that has come about during the past few years has been through the Chicago Pediatric Society, the members of which have given brains and energy and time—often at their own expense—in the endeavor to institute a program.

I am much perturbed about the present situation. Two important developments have recently given impetus to our thinking and planning. The first is the Illinois state law which requires that the Board of Education provide physical examinations of children in elementary schools. The second is the Chicago-Cook County Survey which recommended that school examinations as required by law be promptly extended to all public schools in the Chicago area. Mr. Pritzlaff stated that the cost would be so great that there are not sufficient funds to take care of this program. My answer is that with an organized program the solution might be found, because it is not so much a matter of funds as a matter of the way available funds are spent. If we took the money it now takes to educate laggards who have physical defects, if we took into account vital capacity dissipated because of illness, if we took into account what it costs to keep a sick child going—and put all that money into a fund, we should have enough. I think nothing is impossible to a group that has the will.

How many doctors do we have available to conduct even a pilot examination? None. We have barely enough to do the work with contagious diseases in the hospitals.

The solution of the problem is not so hard if you follow a formula. There used to be 3 or 4 deaths a day in Chicago from diphtheria; last year there were 3.

Years ago there were hundreds of deaths from typhoid fever; last year there was 1. Each of these health problems had a formula applied; they were exposed to the cleansing light of universal knowledge. It is a matter of education of the public, of stirring things up to get your program started and eliminating public ignorance and public indifference.

DR. HENRY G. PONCHER: We are all agreed on the defects in the school program of health examination. Who is responsible for this defect? I think we must face the question frankly and admit our shortcomings. We should like to know from an enlightened group such as we have here just why these conditions exist. It may be that we are not responsible, but who specifically is?

Dr. Hyman will discuss the suggested program based on the recommendations of the Chicago-Cook County Health Survey.

DR. SAMUEL HYMAN (Chief Medical Officer, Department of Health, Chicago): These recommendations necessarily deal with public health principles as applied to a school health program. Translation of such principles into a detailed program in the field will require support of competent and interested groups, such as the Chicago Pediatric Society. Discovery and correction of defects are of primary importance. Parents should be encouraged to take their children to their own physicians for such examination and correction, if possible. For those children not examined by their own physicians, physical examinations should be provided in the school.

The parents should be present at such examinations, if possible. They cooperate when they understand the importance of a child's problem. Prompt and determined action by parents eliminates the necessity for repeated home visits by nurses or repeated reminders to urge the parents into action. Furthermore, the teacher also is better able to understand the child when she fully understands his health status and health problems.

Adequate facilities for examinations should be provided in the schools, including examining tables, audiometers and visual testing apparatus. Regardless of how these physical examinations are done, there must be an adequate follow-up system for correction of discovered defects; there must also be requisite quality and quantity of facilities to take care of discovered defects. Parents should be referred to private physicians for remedial care of the children. Here, of course, the presence of the parent at the examination will help toward solving the problem, as well as toward obviating the necessity for repeated follow-up visits. The record of physical examination should be kept in the school, so that doctors, nurses and teachers may continue to record facts and suggestions on the child's health. The record should be cumulative and follow the child from grade to grade and school to school, just as does his scholastic record.

A particularly important field is psychologic and psychiatric guidance for children. The nutritional service is only on the threshold of its vast possibilities. Health propaganda against a particular disease has its place, but a sound policy of health education must aim at promotion of positive health in its modern conception of the entire personality, physical and mental.

The health program must convince the child and his parents of the necessity of observing fundamental health rules, securing such knowledge, develcping such habits and adopting such attitudes and ideals as will promote physical, mental and emotional well-being. The problem of environment includes playgrounds that are ample in space and free from hazards, with good sanitation and safety from accidents. Within the school, ventilation, heating and sanitation of lunchrooms are problems that require technical study and supervision. Seating and lighting

are of special significance. Also, in connection with environment, examination of school teachers, especially for tuberculosis, is important.

The organization and administration of such a comprehensive program must of necessity include the assistance and guidance of all interested organizations. It is not a one man or one organization job; it requires the coordination of all interested agencies, and the Chicago Pediatric Society because of its pioneer work in child health is, of course, of paramount importance in the establishment of any such program.

DR. WINSTON TUCKER (Health Commissioner, Evanston, Ill.): Many phases of school health have been covered, but I should like to present a few ideas. So far as a healthful school environment is concerned, I need say only this. Parents have the right to expect good schools which are clean, properly ventilated and lighted, with adequate toilet and hand-washing facilities. These are minimum standards which should be provided in all schools.

With reference to medical examinations, I feel that the school is not the proper place to conduct medical examinations of school children. The most satisfactory place is the office or clinic of a private physician, one who knows the child best and who can do a careful and thorough examination. A parent should be present at the time of examination in order that the examining physician may discuss the health of the child with the person most concerned. In fourteen years of experience in public health administration, I have not yet seen satisfactory examinations in a summer roundup. The large number of children and the attendant confusion are not conducive to a good medical examination.

We should make parents aware of their responsibility for good health in their children and inform them that their private physician can best examine their children. This type of school health program has been functioning well in Detroit for many years. Parents tend to want the school to do everything these days; they expect someone else to teach children courtesy, cleanliness and how to get along with others, all of which are really the basic responsibility of the home. There are parents who cannot afford to send the child to a private physician, but Chicago has adequate facilities through which children from indigent and low income groups are eligible for medical service.

I think there should be a physician with special training in public health administration in charge of the entire school health problem, including physical education and instruction in health. The medical administrator and the physical education staff should work together to plan the whole program. In Chicago there should be several health educators on the school health staff, who can serve as consultants to teachers and plan courses in health subjects for the teaching personnel. With an adequate number of properly trained public health nurses for work in the schools, the staff of the school health service will be complete. The nurse comes in contact with school children most frequently and is the one to serve on the front line with teachers, parents and physicians to carry out the policies and program of the school health administrators.

The health service staff should be paid by the school board, and the administrator should be responsible to the superintendent of schools. The function of the department of health is to serve on a cooperative and consultative basis but not to administer the school health program. The chief function of the school health service is to teach children how to develop and retain good health at all times, a task which is primarily the responsibility of the schools. A well organized school health service can work out a program of medical examinations in cooperation with private physicians. The chief health administrator should occupy an

important place in the school system, preferably next in rank to the superintendent and should serve as consultant to the principals, advisers and curriculum planners.

Illinois law requires that school children receive four medical examinations during their school years. In Evanston, new pupils are enrolled in May prior to the opening of school in September. This gives the opportunity to apprise the parent of the need for examination on the child's admission to school. Forms for medical and dental examinations are given to the parent, with instructions to have the examinations completed during the summer. This procedure has functioned very well, and from 90 to 95 per cent of new students are examined by private physicians before entering school; in certain schoolrooms 100 per cent of the children have been so examined. This is adequate evidence that such a program actually works, when the school health staff is able and willing to devote the time required to provide parents with proper health instruction.

Teaching of healthful living can best be done by teachers who have professional training in methods of health instruction. Today, only one teacher in ten is qualified to teach basic principles of good hygiene and sanitation. When most teachers went to normal school or college this subject was not included in their classes. Now, students in colleges, universities and normal schools have the opportunity to take such courses and are prepared to interpret good health habits to pupils. Pupils should learn to wash their hands before eating and after using the toilet, to take a bath three times a week and to change underwear and hose frequently. They should be taught the basic principles of proper nutrition and what constitutes a well balanced meal. They should understand the importance of having breakfast before coming to school. This teaching requires much repetition which cannot be done in a short time.

The subject of teacher health should include a complete preemployment medical examination and annual examinations thereafter by a private physician selected by the teacher. This should include a roentgenogram of the chest, urinalysis and a blood test for syphilis. When teachers understand the importance of good health for themselves, they will do much better in teaching health to school children and will serve as examples as well.

What is the private physician's part in this program? The school sends the medical examination forms to him and says essentially: "You have had this child under your supervision since he was born, and we should like a brief summary of your medical examination for the school records." There are far too many different record forms, and the physician may be asked to complete six different types in one day. We have developed a form which is used in all grade schools in Evanston; it is cumulative from kindergarten through eighth grade and follows the child from school to school. Children are examined when they enter school, at fourth grade, at seventh grade and when they enter high school. I suggest that an examination form be developed by the Chicago Medical Society and the Chicago Pediatric Society and recommended for use in all schools in the Chicago area.

Aside from checking height, weight and vision, school children do not need to be examined every year. This checking can be done in school by the teacher or by older pupils under the teacher's supervision, and it gives them a specific opportunity for participation in the health program. Those who have defects, or those whom physicians refer for special attention, such as those with cardiac disease, crippled children and those with defective vision or hearing, as well as those in whom an optimum amount of correction has been done, can be given special attention by

the school health service staff. The health service staff and the teachers can thus concentrate on teaching healthful living, while medical supervision is provided by a private physician selected by the family.

DR. HENRY G. PONCHER: Dr. Munns, will you discuss your experience with the school health program and the suggestions you may have so far as school health examinations are concerned?

DR. GEORGE F. MUNNS, Winnetka, Ill.: On the North Shore we have been fortunate to have men like Dr. Tucker and Dr. H. A. Orvis, of Winnetka, who head the health departments and who are greatly interested in the school health program. As a result, an effective program has been developed in the North Shore suburbs. As Dr. Tucker said, it is a state law that each child should be examined every four years. As you know, pediatricians feel, and the American Academy of Pediatrics has put itself officially on record to the effect, that each school child should be examined once yearly. Within a three or four year interval too many things can happen to a child which may be serious and which might be avoided if a yearly examination is given. However, in some communities there may be factors which make that difficult. I should say that the majority of children in Winnetka, Kenilworth and Glencoe are examined at least once each year.

In general, it is possible in communities the size of these suburban areas to educate parents well concerning the value of regular check-up examinations, through the school, through propaganda in the press and through physicians themselves. Physicians must cooperate to the fullest extent. In two schools in Winnetka, and probably in many others, 80 per cent of the children were examined in physicians' offices. That is what we have encouraged, just as Dr. Tucker has in Evanston. At one time we performed most examinations in the schools; a group of three or four physicians would go to the school at a designated time, and a chosen group of children was examined. Those examinations were always most unsatisfactory; there was not time to do an adequate examination, and we all felt that the results were hardly worth the time and expense. Hence, we urged that examinations be done in the office, and those children who could not afford to have this done were examined at the school by physicians who went there at an appointed time to examine a small group, and thus were able to take enough time to make an adequate examination. This plan has worked out well.

Among this group, as I said, 80 per cent were examined in the physicians' offices; the total number in the two schools was about 600 pupils; 62 per cent had no medical or dental defects. That is a pretty good record, an unusual record I should say. We followed up with an immunization program which has been effective. For instance, 96 per cent of these children had been immunized to diphtheria, 95 per cent to smallpox, 80 per cent to whooping cough, 65 per cent to tetanus and 27 per cent have had tuberculin skin tests. These figures demonstrate fairly well that a definite program of regular health examinations will really give beneficial results.

One thing I should like to mention particularly is the question of school health examination forms. This is serious from the physician's point of view, particularly when he is examining many children. In the course of an afternoon, four to eight different forms may come into the office to be filled out. In the summer, there may be not only the school examination form but a camp examination form and the office record. By the time one is through with this clerical work one feels one needs about five secretaries. The unforunate thing is that the physician must do it all himself. I am pleading, therefore, that, in the community where

you have influence you urge that a proper and adequate type of form be prepared and, if possible, standardized over a wide area. A satisfactory form should meet certain standards; it should be clear, concise and easily readable; it should be compact to enable easy review, transcription and use for research where permanent records are kept. Only pertinent information should be sought and there should be space enough for detailed description of a defect when necessary.

I have here ten different examination forms which may come to any physician on the North Shore, most of which do not meet the aforementioned standards. The Winnetka school form, also used by Kenilworth and Glencoe, has been designed for easy readability; it is well centered, and easy to fill out. In your own communities, if you intend to prepare such forms, try to set up one which can be read and filled in easily by the physician and transcribed easily by the school. I fully agree with Dr. Tucker and Dr. Hyman that these yearly records should be kept in permanent form, that they should be followed through the school years and that they should be in a form that may be transferred to any other school the child may attend.

DR. HENRY G. PONCHER: Dr. Reichert, will you tell us of the situation in Chicago schools, your experience with school health examinations and any positive suggestion you may have?

DR. JOHN L. REICHERT: Maxwell (Administration of School Health Service, *School Life* **30**:1 [May] 1948) showed that the most effective school health program is one administered and operated by the school system with the aid of the health department. The program in Chicago is based on the legal requirement of the state. Because of financial limitations, there are gaps in such a program, gaps that must be filled by volunteer agencies, including physicians. While the role of the physician includes educational services, such as talks to laymen, personal contacts and the giving of advice, his most important function is his active participation in physical examinations and remedial work. This is the most important part of any health program, since the entire program can be no better than the quality of the examination and the thoroughness of the follow-up work.

Lack of facilities in the school system and in the health department for this work led the Parent-Teachers Association to take over and develop the summer roundup, an annual period of examinations conducted on an entirely voluntary basis and with, usually, indifferent help from physicians. While the results have been far from complete (less than 25 per cent of the 30,000 entering children are examined, and about one half of the remediable defects are corrected), it is a remarkably good result for an organization designed as a liaison and educational group. It is felt that the program can be more efficiently administered by the school system and the health department, with the cooperation of physicians and dentists and with the Parent-Teachers Association functioning as a coordinating agency.

Pilot programs have shown that in self supporting families the examination should be done by the family physician, on a private patient basis, with the report sent to the school. In families of the lower economic levels it is more efficient to have examination done at the school. All the agencies involved, the Parent-Teachers Association, the dentists, the school system and the physicians, have agreed in principle that doctors doing examinations should be compensated. The amount must depend on the economic level of the community. Physicians are willing to donate their services to indigent families, but not in instances in which compensation is justified. The school examinations can be done most efficiently by teams of examiners, consisting of a dentist, physician, otolaryngologist, oph-

thalmologist, orthopedic surgeon, dermatologist and psychiatrist. Some special examinations can be done better at the district rather than the local level in screened groups of children. All the examiners must be thoroughly briefed in the scope and technic of examination. Means of giving such instruction have been set up on a citywide basis. A simple, practical examination form is being developed and will be ready before the next summer roundup.

The purpose of such a program is the discovery and correction of defects. Without this the entire program is valueless. The compilation of a list of the remedial agencies throughout the city which meet the situation at all economic levels is, therefore, a vital part of the program. This is being done with the aid of the social agencies.

All these projects have been tried before in Chicago sporadically, on a local level and with varying success. With the cooperation of all organizations the program is being centralized on the city level. A unit has been set up in the offices of the Chicago Medical Society through which all activities of physicians will be channeled. Each of the other three agencies involved has a similar unit, so that the entire program will be operated by four persons instead of by numerous local groups. The local groups will be kept informed of all activities, and no project will be instituted without consultation with the local chairmen.

The medical group feels that the program shows promise of success due to its centralization and to the splendid cooperation we have had from Mr. Hunt.

DR. HENRY G. PONCHER: While the audience is submitting their questions, I should like to read a series of questions submitted by Mrs. John Leonard Hancock for the Public School Health Committee of the Citizens Schools Committee.

1. Dr. Maxwell, chief of administration of school health for the United States Office of Education of the Federal Security Agency, reports that figures collected for a study of expenditure per pupil in the field of health promotion by city school systems indicate that in 1946-1947 the Chicago Board of Education spent $187,191 on 332,498 pupils, or $0.56 per child, for health. What did this cover?

2. In a letter dated Sept. 30, 1948, the president of the Chicago Department of Health stated that in 1946 the department expended $330,256, or, as he figures, approximately $0.82 per child in the public and parochial elementary schools, on a school health program. What does this provide? What could it provide?

3. From "Blue Print for a Healthy Community" which summarizes the Cook County Health Survey conducted by the United States Public Health Service from April to October 1946, under the heading "School Health Services—Lacking," is the statement: "Chicago schools, both public and private, are almost completely without a systematized and effective medical and nursing service."

If, in 1946, school and department of health authorities were spending a total of $1.38 per school child on health, was Chicago getting as much as could be expected in health service for that amount? What is being done to correct the situation as regards funds and service?

MR. HEROLD C. HUNT: The figures as they relate to the Chicago Board of Education are misleading in that they reflect practices only in our special schools. I am sure Mrs. Hancock and others are aware that this money was not spent for the health of the normal child. The amount spent merely reflects the program dealing with services of psychologic and psychiatric aid and remedial work in reading. We have practically no financial program that relates to health, save that operated in Mr. Pritzlaff's department, which involves teaching health education method through his personnel.

DR. HERMAN BUNDESEN: So far as the Department of Health is concerned, the money was spent for control of communicable diseases only. That service is of paramount importance because without it we could have no control in the schools.

MR. HEROLD C. HUNT: One thing has not been adequately brought out. We are aware of a job that needs to be done. Who is going to do it? If the State Superintendent of Education so indicates and it is accepted that the job is the responsibility of the Chicago School District, then the responsibility should be borne by the school district and it is my hope and belief that ways will be found to do it. Generally, the legislative bodies that pass these laws make some financial provision for their operation; that was not done. If the people of Chicago want the school district, by mandate or voluntarily, to accept the responsibility, it is up to the people of Chicago to provide the necessary wherewithal.

QUESTION: How far may discipline interfere with emotional health and well-being of a child, for example, prohibiting the use of the toilet in the primary grades?

MR. HEROLD C. HUNT: That type of discipline would negate all concepts of well-being of a child. We shall try to see that such conditions are not repeated. Certainly, the answer is it might lead to complete emotional breakdown.

QUESTION: Is any program of education for teachers in modern concepts of emotional development or mental health of children planned?

MR. HEROLD C. HUNT: We are hoping to set up training courses and ultimately to tie these in with requirements for advancements.

QUESTION: Are any physicians involved in the program of health education in the schools?

MR. HEROLD C. HUNT: Dr. Bundesen stressed the phase of control of communicable diseases. The work of the three or four physicians in Mr. Pritzlaff's organization is primarily examination of employees within the system. I should say little, if anything, at all adequate is being done so far as the use of physicians is concerned.

QUESTION: How do you propose to insure examination by a private physician and transmission of the information to you?

MR. HEROLD C. HUNT: The suggestion has been made that we try to accomplish this through the physician. We might provide for it by sending blanks into the homes, with the emphasis that the teacher should be the health exponent within the system. We must train parents to be better parents than their own parents were. We might call the attention of the parents to the law. The plan should provide for a well qualified, trained staff so that it may be followed up, and there again comes the interpretation of the law.

QUESTION: When the law was passed for examination of school children, why were no funds allocated for this purpose?

DR. HERMAN BUNDESEN: That is a pertinent question, but it would not be good policy to attempt to answer it.

QUESTION: What is being done to stimulate participation of young physicians in public health work?

DR. HERMAN BUNDESEN: The staffs of the medical schools in Chicago, outstanding members of the profession, are giving four year courses; in internships and residencies the public health aspect of medicine is being constantly stressed. Members from the Department of Health constantly visit schools and address classes. A weekly course is held by Dr. Morris Fishbein at one of the universities.

So far as the communicable disease aspect is concerned, that is handled at Municipal Contagious Disease Hospital, one of the greatest of its kind in the nation. It was taken over about twenty years ago by the four medical schools, which supervise the staff and determine the policies.

QUESTION: Dr. Hyman stated that the records of physical examinations should be kept in the schools on forms on which doctor, nurse and teacher can keep records; what records does he refer to?

DR. SAMUEL HYMAN: I referred to records of the physical examination of each child completed by the physician who is to do the work in the schools.

QUESTION: Does he infer that the record form of the Parent-Teachers Association is acceptable for follow-up work?

DR. SAMUEL HYMAN: That problem should be studied by various groups so as to evolve one form that will answer the needs of all those interested in the program.

QUESTION: To which nurses does he refer in the handling of these records?

DR. SAMUEL HYMAN: I referred to the nurses in schools. As a matter of fact, we have not given enough credit to nurses. They are doing excellent work, not only with the children but with the families and homes. One recommendation of the Cook County Health Survey was that there should be adequate numbers of nurses working in schools, homes and clinics on problems of children.

QUESTION: What is wrong with the relationship of the family physician and the school?

MR. A. H. PRITZLAFF: That and similar questions were discussed at a meeting sponsored by the American Medical Association in Highland Park, Ill., last year. A physician does not know how much he should divulge about a patient, particularly since many different persons may contact him from a given school. It was felt that if one person was designated to contact physicians and that the physicians were informed of the purpose of the information sought, a working relationship could be developed. If schools explained the nature of the program and modifications possible to provide for individual differences and needs, it was felt that there would be fewer requests from physicians for excuses from the physical education program. Again because of lack of knowledge, physicians frequently approve a boy's participating in a strenuous sport and request exclusion from one less strenuous. Cooperation should be encouraged.

DR. JOHN L. REICHERT: As to the compensation the physician should receive for examinations in a health program, the Chicago Medical Society decided on the following schedule: $15 for the first hour and $5 for every hour thereafter. Several communities have set $1 per child, divided equally among the examiners. I do not think the amount is important. Examiners simply are not willing to have the value of their services placed at zero.

DR. HENRY G. PONCHER: We hope that this discussion will not be considered merely as a part of a program of the Chicago Pediatric Society. I hope it will stimulate every one concerned with school health.

News and Comment

NOTICES

Hygeia Renamed.—The board of trustees of the American Medical Association has authorized the renaming of the Association's health magazine, *Hygeia*. The new name will be *Today's Health*. The change will be made with the issue of March 1950.

Course on Problems in Pediatrics.—Among the postgraduate courses to be offered in 1950 at the Medical Center, San Francisco, by the Medical Extension of the University of California Medical School, is one on special problems in pediatrics, which will be given February 6 to 10.

Meeting of the American Academy for Cerebral Palsy.—The American Academy for Cerebral Palsy will hold its annual meeting in New York at the Waldorf-Astoria Hotel from 2 to 5 p.m. on Feb. 17 and from 9 a.m. to 12 m. on Feb. 18, 1950, immediately after the meeting of the American Academy of Orthopaedics. Scientific sessions will be open to visiting orthopedists and to any other physicians interested in the problem of cerebral palsy.

Examinations of American Board of Pediatrics, Inc.—Written examinations under local monitors will be held by the American Board of Pediatrics, Inc., on Thursday, Jan. 12, 1950, from 2 to 4 p. m. This is the only written examination that will be given during 1950. The next oral examination will be in Richmond, Va., on Feb. 10, 11 and 12, 1950, in Philadelphia on March 31, April 1 and April 2, 1950, and in San Francisco, June 23, 24 and 25, 1950.

GENERAL NEWS

Course in Pediatrics for General Physicians.—A continuation course in pediatrics for general physicians will be presented at the Center for Continuation Study of the University of Minnesota, Minneapolis, Jan. 26 to 28, 1950. The course will be divided into three major divisions: The importance of hereditary and genetic factors in understanding pediatric problems, common dermatologic problems seen in infants and children and common infectious diseases. Dr. Franklin Top, of the Herman Kiefer Hospital, Detroit, will be the visiting faculty member for the course.

PERSONAL NEWS

Dr. Robert A. Strong on the Army Retired List.—Dr. Robert A. Strong, Pass Christian, Miss., an emeritus fellow of the American Academy of Pediatrics and former professor of pediatrics at Tulane University, New Orleans, was placed on the retired list of the Army of the United States with the rank of Colonel on June 29, 1948, after thirty-one years of service.

Book Reviews

The Child in Health and Disease. Edited by Clifford G. Grulee, M.D., and R. Cannon Eley, M.D. Price, $12. Pp. 1,025, with 224 illustrations and 3 plates. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1948.

This is the first new textbook in many years in the field of pediatrics. The seventy-five contributors emphasize the application of modern pediatric knowledge. The editors state in the preface that medical science has outrun the art, and the book is an endeavor to further the practical side. It succeeds admirably in its aim.

The nineteen sections of the book are arranged in logical sequence. The first section, "General Considerations," is divided into chapters on physical and mental growth and development and a chapter on pediatric pathology, the first to be found in a pediatric text, is a good addition. This chapter should be read carefully and would benefit many pathologists who fail to give proper consideration to the typical variations seen in the young patient.

"Nutrition," a section in six chapters, begins with a chapter on the physiology of digestion. This is followed by chapters on nutritional requirements, breast feeding, which is an exceptionally good discussion, nutritional disturbances and vitamin deficiencies. The chapter on artificial feeding is somewhat sketchy, though it includes complete tables regarding composition and caloric content of many artificial foods.

Sections on the newborn infant and prematurity are excellent. Communicable diseases are covered, with an especially good discussion of meningococcic meningitis and poliomyelitis. Acute infections are well discussed. Excellent color plates of the malarial parasite are included. Newer drugs in treatment of malaria than quinacrine hydrochloride (atabrine *di*-hydrochloride®) are not mentioned, though several have been developed.

The material on chronic infections includes consideration of tuberculosis and syphilis. The seventh section, on the circulatory system, including the blood, spleen and lymph nodes, takes in only heart disease and rheumatic fever. It should have included the portions of the eighth section, on the blood and lymph, since all the subjects of these chapters are included under the title of section VII. No fault can be found with any of these chapters, written by Gibson, Poncher, Sanford and Farber.

The rest of the book follows the general pattern of body systems. All the articles are uniformly well done, and without serious errors of either omission or commission. The section on diseases of the nervous system, by Buchanan, Bucy and Bakwin, is outstanding and is the highlight of the book.

Chapters on orthopedics and allergy and diseases of the skin are well presented. The section on the endocrine glands includes an excellent discussion of juvenile diabetes by Priscilla White. Its simplicity and clarity are a great help to those who only occasionally see a diabetic child.

The section on adolescence has a unique chapter on growth, development and physiologic function—which is much needed and exceptionally informative. Disorders of puberty in the female, by Goodrich C. Schauffler, is good. A gratifying inclusion in this section is the Pryor width-weight tables.

Surgical pediatrics, by Coe, has an unusually complete discussion of preoperative and postoperative care and pediatric anesthesia. A section on miscellaneous subjects concludes the book with discussions of poisoning, first aid and pediatric technics. The latter chapter is excellent in its field.

The book is interesting and refreshing. It is easy to read and inclusive enough for any ordinary need. Despite the large number of contributors, there is a uniformity of the whole that shows careful editing. It is well suited both as a textbook for students and as a reference work for the practitioner.

Histopathology of the Peripheral and Central Nervous Systems. Third edition, revised and enlarged. By George B. Hassin, M.D. Price, $8.50. Pp. 612, with 302 illustrations. The Hamilton Press, 4341 N. Meade St., Chicago 34, 1948.

This book is representative of the long labors of Dr. Hassin in the field of neuropathology, during approximately thirty-five years. It is not surprising, then, that the text should be recognized as the outstanding book in the English language on the subject of microscopic pathology of nervous diseases. Nor will the reader be astonished to learn that its author is considered the dean of American neuropathologists and, logically, is the editor of the only journal concerned particularly with this field of investigation.

The text is divided into five parts, the first dealing with general considerations of histology and histopathology of nervous tissues, the second with diseases of the peripheral nerves, the third with those of the spinal cord, the next with those affecting the brain and the final one with staining methods. While this anatomic approach to the problem makes some duplication necessary (since, for example, tumors of the spinal canal are essentially the same as those compromising the cranial space), this is not a serious difficulty. The inflammatory diseases of the dura mater and the traumatic lesions of the brain are rather sketchily dealt with, in contrast to the inflammatory, infiltrative diseases and degenerative diseases, which are so well handled. One misses any reference to neonatal anoxia or, for that matter, to any type of anoxia except that caused by carbon monoxide.

The illustrations are excellent and in abundance; hence most important points are graphically portrayed.

This book is not one for the casual reader. It will not have too great an appeal to the surgeon. But to the pathologist, to the clinician who wants a reference work on histopathology of the nervous system, to one genuinely interested in organic neurology, this text will be an important and essential addition to his working library.

CORRECTION

In the Article in the September issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN entitled "Fibrosis of the Pancreas in Infants and Children: A Statistical Study of Clinical and Hereditary Features," by C. U. Lowe, M.D.; C. D. May, M.D., and S. C. Reed, Ph.D., the following corrections should be made: On page 358, in the legend for chart 3, "table 16" (lines 8 and 9) should read "table 4"; on page 360 the percentages given in parentheses should be omitted, and on page 361, line 7, "a 1:4 chance" should read "a 1 in 4 chance."

Directory of Pediatric Societies *

INTERNATIONAL

SIXTH INTERNATIONAL CONGRESS OF PEDIATRICS

President: Prof. Guido Fanconi.
Secretary: Dr. H. Zellweger, Kinderklinik, Zurich.
American Committee:
President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-General: Dr. L. Emmett Holt Jr., 477 First Ave., New York 16.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. S. G. Ross, 1390 Sherbrooke St. W., Montreal.
Place: Zurich, Switzerland. Time: July 24-28, 1950.

INTERNATIONAL CONGRESS FOR THE PROTECTION OF INFANCY

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

PAN AMERICAN CONGRESS OF PEDIATRICS

President: Dr. Felix Hurtado, Habana, Cuba.

INTERNATIONAL UNION FOR CHILD WELFARE

President: Mrs. Gordon Morier.
Secretary: Dr. Georges Thélin, 43 Quay Wilson, Geneva, Switzerland.

FOREIGN

ARGENTINE PEDIATRIC SOCIETY OF BUENOS AIRES

President: Dr. Martín Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

ASSOCIAÇÃO PAULISTA DE MEDICINA, SECÇÃO DE PEDIATRIAS

President: Dr. Armando de Arruda Sampaio.
First Secretary: Dr. Luis Fontoura y Lauro Machado Oliveira, Caixa Postal 2103, São Paulo, Brazil.
Second Secretary: Dr. Luiz Augusto Monteiro Toledo, Av. Brigadeiro Luiz Antonio 393, 1° Andar, São Paulo, Brazil.
Time: Twelfth of every month, 8:30 p. m.

ASOCIACIÓN PEDIATRICA DE GUATEMALA

President: Dr. Carlos Manuel Monzon, Plazuela Santuario de Guadalupe, Guadalupe.
Secretary: Dr. Maria Isabel Escobar, Casa del Niño no. 1, Guadalupe.

BRITISH PAEDIATRIC SOCIETY

President: Dr. A. G. Maitland-Jones.
Secretary: Dr. Alan Moncrieff, Institute of Child Health, Hospital for Sick Children, Great Ormond St., London W. C. 1.
Place: Windermere.

BULGARIAN PEDIATRIC SOCIETY

President: Dr. L. Ratchew, University Children's Hospital, Wassil Kolarow 46, Sofia.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

CHINESE PEDIATRIC SOCIETY

President: Dr. W. S. Fu, The Shanghai Public Hospital for Children, 11 Hsiang Shan Road, Shanghai, China.
Secretary: Dr. T. F. Su, The Shanghai Public Hospital for Children, 11 Hsiang Shan Road, Shanghai, China.
Time: Concurrent with the annual conference of the Chinese Medical Association.

CZECHOSLOVAK PEDIATRIC SOCIETY

Chairman: Prof. Dr. Jiri Brdlík, 2 Sokolská, Prague II.

DANISH PEDIATRIC SOCIETY

Chairman: Prof. Preben Plum.
Secretary: Dr. Elin Fog, Søllingsvey 17, Charlottenlund, Denmark.

GERMAN PEDIATRIC SOCIETY

President: Dr. H. Kleinschmidt.
Secretary: Dr. F. Goebel, 5 Moorenstrasse, Düsseldorf, Germany (British Zone).
Place: Düsseldorf. Time: September 1949.

HELLENIC SOCIETY OF PEDIATRICS

President: Dr. C. Saroglou, Patission St. 74, Athens, Greece.
Secretary-General: Dr. S. Charocopos, Alexandras Ave. 1, Athens, Greece.

INDIAN PEDIATRIC SOCIETY

President: Dr. K. C. Chaudhuri, 56/2 Creek Row, Calcutta 13.
Secretary: Dr. N. G. Mojumdar, 148 Russa Rd., Calcutta 26.
Place: 67 Dharamtala St., Calcutta 13. Time: Every second and fourth Wednesday of each month.

NEDERLANDSCHE VEREENINGING VOOR KINDERGENEESKUNDE

President: Dr. G. J. Huët, 39 Brediusweg, Bussum.
Secretary: Dr. H. Reerkink, % Sophia Kinderziekenhuis, 160 Gordelweg, Rotterdam.
Place: Children's Hospital or Pediatric Clinic. Time: Three times a year.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICANS OF CHILDREN'S DISEASES

President: Prof. L. F. Meyer, 29 Toelsohn St., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

PEDIATRIC SOCIETY OF NEW ZEALAND

President: Dr. Lawrence Ludbrook, The Lister Building, Victoria Street East, Auckland.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASES IN CHILDREN

President: W. W. Payne.
Secretary: Dr. R. E. Bonham Carter; Dr. I. M. Anderson, 52 Harley St., London.
Place: 1 Wimpole St., London W. 1. Time: Fourth Friday of each month, 4:15 p. m.

SCHWEIZERISCHE GESELLSCHAFT FÜR PÄDIATRIE

President: Prof. Dr. A. Hottinger, Petersplatz 12, Basel.
Secretary: Dr. F. Hauser, Kinderspital, Basel.

SOCIEDAD BOLIVIANA DE PEDIATRIA

President: Dr. Carlos Ferrufino, Casilla 272, La Paz, Bolivia.
Secretary: Dr. Cecilio Abela D., Casilla 272, La Paz, Bolivia.
Place: S. C. I. S. P. Bldg. Time: Every Thursday.

SOCIEDAD CHILENA DE PEDIATRIA

Chairman: Dr. Jose Bauza.
Secretary: Dr. Guillermo Llodra, Merced 565, Santiago, Chile.
Place: Medical Society, Merced 565, Santiago, Chile. Time: 7 p. m., every Thursday.

SOCIEDAD CUBANA DE PEDIATRIA

President: Prof. Agustin Castellanos.
Secretary: Dr. Carlos Hernandez Miyares, Hospital Nuestra Señora de las Mercedes L y 21, Apartado 2430, Habana.
Place: Cátedra de Clinica Infantil, Hospital Nuestra Señora de las Mercedes y Hospital Municipal de Infancia, Habana. Time: 9 p. m., last Wednesday of every month.

SOCIEDAD DOMINICANA DE PEDIATRIA

President: Dr. Jaime Jorge, Jose Joaquin Perez, no. 25, Ciudad Trujillo, R.D.
Secretary-Treasurer: Dr. Alberto Peguero, V., Ave. Bolivar 113, P. O. Box, 464, Ciudad Trujillo, R.D.
Place: Children's Ramfis Hospital. Time: 8 p. m., last Friday of every month.

SOCIEDAD ECUATORIANA DE PEDIATRIA

President: Dr. Alfredo Ceballos Carrión.
Secretary: Dr. Rafael Compte Andrade, P. O. Box 3480, Guayaquil.
Place: Hospital Central. Time: 11:30 a. m., every Friday.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Jesus Avarez de los Cobos.
Secretary: Dr. Luis Torregrosa F.
Place: Hospital Infantil. Time: Last Thursday of every month.

SOCIEDAD DE PEDIATRÍA DE CONCEPCIÓN (CHILE)

President: Dr. Raúl Ortega A., Hospital Clínico Regional, Concepción.
Secretary: Dr. Fidel Urrutia, Hospital Clinico Regional, Concepción.
Place: Hospital Clínico Regional, Concepción. Time: 7:30 p. m., second Tuesday of every month from April to December, inclusive.

SOCIEDAD DE PEDIATRÍA DE CÓRDOBA

President: Dr. Juan Francisco Herrera, Córdoba, Argentina.
Secretary: Dr. Albino F. Dottori, Dean Fumes 2000, Esq. Ocaña (N.), Córdoba, Argentina.
Place: Comite pro Defenso del Niño, Dean Fumes 2000, Córdoba, Argentina.
Time: Once a month.

SOCIEDAD DE PEDIATRIA DEL LITORAL

President: Dr. Jose E. Celoria, Hospital Centenario, Rosario, Argentina.
Secretary: Dr. Gloria Lovell, Hospital Centenario, Rosario, Argentina.

SOCIEDAD DE PEDIATRÍA DE SANTIAGO DE CUBA

President: Dr. Antonio Béguez César, Sagarra 107, Santiago de Cuba.
Secretary: Dra. Susana Texdó Vaillant, Padre Pico 57, Santiago de Cuba.
Place: Colegio Médico. Time: Last Tuesday of every month.

SOCIEDADE PORTUGUÊSA DE PEDIATRIA

President: Prof. Almeida Garrett.
Secretary-Generale: Dr. Cordeiro Ferreira, Hospital de D. Estefania, Lisbon.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRIA

President: Lya Imber Coronil.
Secretary: Dr. Guillermo Tovar, P. O. Box 5, Caracas.
Place: Hospital Municipal de Niños, Caracas. Time: Once a month.

SOCIEDAD YUCATECA DE PEDIATRIA

President: Dr. José Lavalle, Yucatan, Mexico.
Secretary: Dr. Francisco Solís, Yucatan, Mexico.
Place: Hospital del Niño, Yucatan, Mexico.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. G. Heuyer, 1 Ave. Emile Deschanel, Paris 7e, France.
Secretary: Dr. Maurice Lamy, 94 rue de Varenne, Paris 7e, France.
Place: Hôpital des Enfants Maladies, 149 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

SOCIETÉ POLONAISE DE PÉDIATRIE

President: Dr. Jan Bogdanowicz, Dzialdowska 1, Warsaw.
Secretary: Dr. Zofia Leimbach, Mieroslawskiego 9 m.6, Warsaw.

SOUTH AFRICAN PAEDIATRIC ASSOCIATION

Chairman: Dr. Basil Melle, 89 Lister Bldg., 195 Jeppe St., Johannesburg, South Africa.
Secretary-Treasurer: Dr. Seymour Heymann, 17 Lister Bldg., 195 Jeppe St., Johannesburg, South Africa.

SWEDISH ASSOCIATION OF PEDIATRICS

President: Prof. A. Lichtenstein, Crown Princess Louise's Children's Hospital, 30 Polhemsgata, Stockholm.
Secretary: Dr. K. A. Melin, Farjestadsvägen 16, Ängby.

SWEDISH MEDICAL SOCIETY, SECTION FOR PEDIATRICS AND SCHOOL HYGIENE

President: Dr. R. Hybbinette, Kommendorsgatan 3, Stockholm.
Secretary: Dr. B. Broman, Eriksbergsgatan 1A, Stockholm.
Place: Various clinics and hospitals in Stockholm and Uppsala. Time: Second Friday of each month (except summer).

URUGUAYAN SOCETY OF PEDIATRICS

President: Dr. Héctor C. Bazzano.
Secretary: Dr. José M. Portillo.
Place: Club Medico del Uruguay, Avenida Agraciada 1464 (Piso 13), Montevideo.

VIENNA PEDIATRIC SOCIETY

President: Prof. Dr. A. Solé, Karolinen-Kinderspital, Sobieskigasse 31, Vienna 9.
Secretary: Doz. Dr. Asperger, Universitäts-Kinderklinik, Lazarettgasse 14, Vienna 9.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. Woodruff L. Crawford, 321 W. State St., Rockford, Ill.
Secretary: Dr. Margaret Mary Nicholson, 1801 Eye St. N. W., Washington, D. C.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. Warren R. Sisson, 319 Longwood Ave., Boston 15.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Annual Meeting: Place: San Francisco. Time: Nov. 14-17, 1949.

AMERICAN HOSPITAL ASSOCIATION, MASSACHUSETTS HOSPITAL ASSOCIATION

Chairman: Dr. Frank Wing, Boston.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly 79, Mass.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Valjean Cooke, 8700 Argyle Ave., St. Louis.
Secretary-Treasurer: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. P. E. Williams, 193 James St. S., Hamilton, Ontario.
Secretary-Treasurer: Dr. R. L. Denton, 1615 Cedar Ave., Montreal.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Francis F. Schwentker, 601 N. Broadway, Baltimore, Md.
Secretary-Treasurer: Dr. Robert Ward, Bellevue Hospital, New York 16.
Place: French Lick, Ind. Time: 1950.

SECTIONAL

Intermountain Pediatric Society

President: Dr. Spencer Snow, 75 S. Main St., Salt Lake City.
Secretary-Treasurer: Dr. Esther Gross, 202 E. South Temple St., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

President: Dr. Henry E. Gallup.
Secretary-Treasurer: Dr. Harry Shwachman, 300 Longwood Ave., Boston.
Time: Four meetings a year. Next meeting, Sept. 28, 1949.

North Pacific Pediatric Society

President: Dr. Clarence L. Lyon, 407 Riverside Ave., Spokane 8, Wash.
Secretary: Dr. Aldis B. Johnson, 515 Cobb Bldg., Seattle, Wash.

Northwestern Pediatric Society

President: Dr. Paul Bancroft, 909 Sharp Bldg., Lincoln, Neb.
Secretary-Treasurer: Dr. Northrop Beach, 1009 Nicollet Ave., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Rocky Mountain Pediatric Society

President: Dr. William D. Rothwell Jr., Republic Bldg., Denver.
Secretary: Dr. Edwin T. Williams, 1850 Gilpin St., Denver 6.
Place: Children's Hospital of the Colorado General Hospital. Time: Monthly from October to June.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Carroll M. Pounders, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. Samuel F. Ravenel, 371 N. Elm St., Greensboro, N. C.

STATE

Alabama Pediatric Society

President: Dr. W. A. Daniel Jr., 115 S. Union St., Montgomery 5, Ala.
Secretary-Treasurer: Dr. D. B. Monsky, 905 Norman Bridge Rd., Montgomery 6, Ala.
Place: Montgomery, Ala. Time: September 1949.

Arizona Pediatric Society

President: Dr. Carl A. Holmes, 1401 N. 7th Ave., Phoenix.
Secretary-Treasurer: Jacob M. Sobol, 607 Heard Bldg., Phoenix.
Place: Phoenix or Tucson. Time: On call.

Arkansas State Pediatric Association

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

California State Medical Society, Section on Pediatrics

Chairman: Dr. Alice Potter, 1418 Ninth Ave., San Francisco 22.
Secretary: Dr. Carl Erickson, 595 E. Colorado, Pasadena.

Florida State Pediatric Society

President: Dr. Edgar W. Stephens, 910 Harvey Bldg., West Palm Beach.
Secretary: Dr. Hugh A. Carithers, 2000 Park St., Jacksonville 4.
Place: Concurrent with state association convention and fall meeting.

Georgia Pediatric Society

President: Dr. Lee Bivings, 20 Fourth St. N. W., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Place: Atlanta. Time: At time of annual state meeting.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB OF CONNECTICUT

President: Dr. H. L. F. Locke, 179 Allyn St., Hartford, Conn.
Secretary: Dr. L. W. Minor, 119 Main St., Middletown, Conn.

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Eugene T. McEnery, 4458 W. Madison St., Chicago 24.
Secretary: Dr. George L. Drennen, Jacksonville, Ill.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Matthew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

IOWA PEDIATRIC SOCIETY

President: Dr. Charlotte Fisk, 1201 Equitable Bldg., Des Moines 9.
Secretary-Treasurer: Dr. James Dunn, Davenport Bank Bldg., Davenport.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. William C. Rivenbank, 1448 Louisiana Ave., New Orleans 15.
Secretary-Treasurer: Dr. Bertha Wexler, 3439 Prytania St., New Orleans 15.

MEDICAL SOCIETY OF THE STATE OF NEW YORK, PEDIATRIC SOCIETY

Chairman: Dr. Thurman B. Givan, 115 Remsen St., Brooklyn 2.
Secretary: Dr. Reginald A. Higgons, Port Chester.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, PEDIATRIC SECTION

Chairman: Dr. Waldo E. Nelson, Temple University, Philadelphia 40.
Secretary: Dr. Carl C. Fischer, 100 W. Coulter St., Philadelphia 44.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. H. J. Lewis, 2956 Biddle Ave., Wyandotte.
Secretary: Dr. Robert H. Trimby, 122 W. Hillsdale, Lansing.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Place, Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. George Clark, 1817 Vinton St., Omaha.
Secretary-Treasurer: Dr. Michael Crofoot, 1407 Medical Arts Bldg., Omaha 2.
Place: Children's Memorial Hospital. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NEW HAMPSHIRE PEDIATRIC SOCIETY

President: Dr. Thomas B. Walker, Porthmouth.
Secretary-Treasurer: Dr. Ursula G. Sanders, Concord.

NEW JERSEY MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Israel J. Wolf, 231 E. 31st St., Paterson.
Secretary: Dr. N. T. Crane, 147 E. 7th St., Plainfield, N. J.

NEW MEXICO STATE PEDIATRIC SOCIETY

President: Dr. M. K. Wylder, 221 W. Central Ave., Albuquerque.
Secretary-Treasurer: Dr. Ly Werner, 221 W. Central Ave., Albuquerque.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. S. S. Saunders, High Point, N. C.
Secretary: Dr. S. C. Dees, Durham, N. C.

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. William C. Deamer, 3 Fifth Ave., San Francisco 18.
Secretary: Dr. A. L. Gleason, 1066 Longridge Rd., Oakland 10.
Place: San Francisco. Time: Second Thursday of February, April, September and November.

NORTH DAKOTA PEDIATRIC SOCIETY

President: Dr. R. E. Dyson, Northwest Clinic, Minot, N. D.
Secretary-Treasurer: Dr. William J. Ball, Northwest Clinic, Minot, N. D.
Place: Fargo Clinic, Fargo, N. D. Time: October 15.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. J. B. Snow, 625 N. W. 10th St., Oklahoma City.
Secretary: Dr. Bertha Levy, 1200 N. Walker St., Oklahoma City.
Place: With Oklahoma State Medical Association. Time: Annual Meeting.

PHILIPPINE PEDIATRIC SOCIETY

President: Dr. Alberto V. Tupas, Philippine General Hospital, Manila, Philippines.
Secretary: Dr. Artemio P. Jongco, Philippine General Hospital, Manila, Philippines.
Place: Philippine General Hospital. Time: Every two months.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. B. Owen Ravenel, 95 Rutledge Ave., Charleston 16.
Secretary-Treasurer: Dr. John R. Harvin, 206 N. Sumter St., Sumter.

TENNESSEE PEDIATRIC SOCIETY

President: Dr. W. O. Vaughan, 2103 Hayes St., Nashville 5.
Secretary-Treasurer: Dr. C. Barton Etter, 1678 Peach, Memphis 12.
Place: Chattanooga. Time: Second Monday in April.

TEXAS PEDIATRIC SOCIETY

President: Dr. John E. Ashby, 3610 Fairmount, Dallas, Texas.
Secretary: Dr. M. C. Carlisle, 1410 Austin Ave., Waco, Texas.
Place: Fort Worth. Time: Oct. 6-7, 1949.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. C. P. Brown, 142 W. York St., Norfolk.
Secretary: Dr. E. Berkeley Neal, 303 Washington Ave. S. W., Roanoke.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. Thomas G. Folsom, 1139 Fourth Ave., Huntington.
Secretary: Dr. Warren J. Parsons, 425 Eleventh St., Huntington.

WISCONSIN STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. M. G. Peterman, 411 E. Mason St., Milwaukee 2.
Secretary: Dr. L. M. Simonson, 1001 N. 8th St., Sheboygan.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. John Hart Davis, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. Francis F. Silver, 9400 Euclid Ave., Cleveland.
Place: Allen Memorial Medical Library. Time: 8:15 p. m., October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. A. L. Chute, 170 St. George St., Toronto, Canada.
Secretary: Dr. John Fletcher, 262 St. Clair St. W., Toronto, Canada.
Place: Academy of Medicine. Time: 8:30 p. m., third Thursday of each month.

BALTIMORE CITY MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. J. Edmund Bradley, University Hospital, Baltimore 1.
Secretary: Dr. Wilson Grubb, 4 E. 33rd. St., Baltimore 18.

BRONX PEDIATRIC SOCIETY

President: Dr. Nathan M. Greenstein, 1488 Metropolitan Ave., New York.
Secretary: Dr. George Weiss, 790 Grand Concourse, New York 51.
Place: Morrisania City Hospital. Time: 8:30 p. m., second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Walter R. Coles, 604-2d St., Brooklyn.
Secretary: Dr. Bernard Benjamin, 845 Park Pl., Brooklyn 16.
Place: Granada Hotel. Time: 8:45 p. m., fourth Wednesday of February, March, April, October and November.

Buffalo Pediatric Society

President: Dr. Douglas P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo 9, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

Central New York Pediatric Club

President: Dr. T. Wood Clarke, 7 Cottage Place, Utica.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Tuesday of April and October.

Chicago Pediatric Society

President: Dr. Arthur F. Abt, 104 S. Michigan Blvd., Chicago 3.
Secretary: Dr. Alfred S. Traisman, 6349 N. Clark St., Chicago.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May inclusive.

Cincinnati Pediatric Society

President: Dr. John H. Hunt, Kemper Lane Bldg., Cincinnati.
Secretary: Dr. William F. Hunting, 6048 Montgomery, Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati. Time: On call.

Dallas Pediatric Society

President: Dr. Guy Hacker, 5711 Goliad St., Dallas.
Secretary-Treasurer: Dr. George R. Branch, 4325 Cole Ave., Dallas.
Place: Children's Hospital of Texas and Bradford Memorial Hospital. Time: 1 p. m., third Saturday and 8:30 p. m., the first Tuesday of each month.

Detroit Pediatric Society

President: Dr. Wilfred D. H. Nolting, 16840 E. Warren, Detroit.
Secretary: Dr. Ruben Meyer, 938 Maccabees Bldg., Detroit.
Place: Variable. Time: Five times annually.

Fort Worth Pediatric Society

President: Dr. Frank Cohen, 712 S. Henderson, Fort Worth, Texas.
Secretary: Dr. H. H. Womack, 1422 Pennsylvania, Fort Worth, Texas.
Place: Welch and West Restaurant. Time: Third Friday of each month.

Honolulu Pediatric Society

President: Dr. Donald Marshall, Medical Group, Honolulu.
Secretary-Treasurer: Dr. Teruo Yoshina, 1221 Victoria St., Honolulu

Houston Pediatric Society

President: Dr. Edward O. Fitch, 3720 Fannin St., Houston, Texas.
Secretary: Dr. Thomas J. Donovan, 3506 Sunset Blvd., Houston 5, Texas.
Place: River Oaks Country Club. Time: 7:30 p. m., last Tuesday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1624 Professional Bldg., Kansas City.
Secretary: Dr. Leland Speer, 1022 Hoel Parkway, Kansas City.
Place: Kansas City General Hospital. Time: On call.

Knoxville-Oak Ridge Pediatric Society

President: Dr. Henry S. Christian, 205 Medical Arts Bldg., Knoxville, Tenn.
Secretary: Dr. John Egglestor, Oak Ridge Hospital, Oak Ridge, Tenn.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Elena Boder, 1830½ Lucille Ave., Los Angeles 26.
Secretary-Treasurer: Dr. Robert Simonds, 267 S. Beverly Dr., Beverly Hills, Calif.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

MEDICAL SOCIETY OF THE COUNTY OF KINGS AND THE ACADEMY OF MEDICINE OF BROOKLYN, PEDIATRIC SECTION

President: Dr. Samuel Silber, 865 Park Place, Brooklyn.
Secretary: Dr. Jacob J. Lichterman, 1433 Union St., Brooklyn 13.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., fourth Monday of each month.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION ON PEDIATRICS

President: Dr. John Washington, 2032 Belmont Rd. N.W., Washington, D. C.
Secretary-Treasurer: Dr. George Maksim, 1418 Good Hope Rd. S. E., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N.W. Time: Spring and fall.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. C. Barton Etter, 1678 Peach, Memphis 12, Tenn.
Secretary-Treasurer: Dr. Jacob Danciger, 188 S. Bellevue Blvd., Memphis 4, Tenn.
Place: University Center, 4 S. Dunlap. Time: 7 p. m., second Tuesday of every month.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. James Conway, 1721 E. Lake Bluff Blvd., Milwaukee 11, Wis.
Secretary-Treasurer: Dr. Walter Polacheck, 425 E. Wisconsin Ave., Milwaukee 2, Wis.
Place: City Club of Milwaukee. Time: Second Wednesday in February, April, June, October and December.

NASHVILLE PEDIATRIC SOCIETY

President: Dr. John M. Lee, Doctors Bldg., Nashville, Tenn.
Secretary: Dr. Dan S. Sanders Jr., 2103 Hayes St., Nashville, Tenn.
Time: Third Thursday of every month.

NEW YORK ACADEMY OF MEDICINE, SECTION ON PEDIATRICS

Chairman: Dr. John Dorsey Craig, 120 E. 75th St., New York 21.
Secretary: Dr. Morris Greenberg, 143 W. 87th St., New York.
Place: New York Academy of Medicine, 2 E. 103rd St. Time: Second Thursday of each month from November to May, inclusive, 8:30 p. m.

OKLAHOMA CITY PEDIATRIC SOCIETY

President: Dr. Bertha M. Levy, 717 N. W. 22d St., Oklahoma City 3.
Secretary: Dr. C. M. Bielstein, 301 N. W. 12th St., Oklahoma City 3.
Place: Oklahoma Club. Time: On call.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Aims C. McGuinness, 1740 Bainbridge St., Philadelphia 46.
Secretary: Dr. F. H. Harvie, 133 S. 36th St., Philadelphia 4.
Place: College of Physicians, 19 S. 22nd St. Time: 8:30 p. m., second Tuesday from October to May, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. J. A. Gilmartin, 3708–15th Ave., Pittsburgh.
Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh 13.
Place: Municipal Hospital, Pittsburgh. Time: Second Friday in October, December, February and April.

QUEENS PEDIATRIC SOCIETY

President: Dr. Henry A. Reisman, 88-03 146th St., Jamaica, L. I.
Secretary: Dr. Moe Goldstein III, 3a 76th Ave., Forest Hills, L. I.
Place: Forest Hills, N. Y. Time: Third Monday of October, February, April; first Monday of December.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Thomas S. Chalkley, 421 W. Grace St., Richmond 20, Va.
Secretary-Treasurer: Dr. John Paul Jones, 810 W. Franklin St., Richmond 20, Va.
Place: Medical College Hospital. Time: 8 p. m., third Thursday of each month, except June, July and August.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. Jerome Glaser, 85 San Gabriel Dr., Rochester 10, N. Y.
Secretary-Treasurer: Dr. Daniel B. Peeler, 1162 Lake Ave., Rochester 13, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee.
Time: Third Friday of each month from October to May.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Merl J. Carson, 500 S. Kingshighway, St. Louis.
Secretary-Treasurer: Dr. Jackson K. Eto, 734 Missouri Theatre Bldg., St. Louis 3.
Place: Hotel Branscome. Time: Second Thursday of each month from October to May, inclusive, 6:30 p. m.

SAN ANTONIO PEDIATRIC SOCIETY

President: Dr. Lucius Hill, 328 Medical Arts Bldg., San Antonio 5.
Secretary-Treasurer: Dr. Edith M. Bonnet, 228 Medical Arts Bldg., San Antonio 5.
Place: Bexar County Medical Library. Time: 7:30 p. m., first Tuesday of every month.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Sherod M. Billington, Medical Dental Bldg., Seattle 1.
Secretary: Dr. Jack M. Doctor, 738 Broadway, Seattle 22.
Place: College Club. Time: Fourth Friday of each month from September to June at 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Chester I. Mead, 1930 Truxton Ave., Bakersfield, Calif.
Secretary: Dr. Clement H. Maloney, 416 N. Bedford Dr., Beverly Hills, Calif.
Place: University Club of Los Angeles. Time: 6:30 p. m., second Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Ernest H. Watson, University Hospital, Ann Arbor.
Secretary: Dr. Harry A. Towsley, 1313 E. Ann St., Ann Arbor.

WACO PEDIATRIC SOCIETY

President: Dr. M. C. Carlisle, 1410 Austin Ave., Waco, Texas.
Secretary: Dr. F. W. Hoehn, 1422 Austin Ave., Waco, Texas.
Place: Provident Hospital, 1725 Colcord, Waco, Texas. Time: Third Thursday of each month.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRICS SECTION (NEW YORK)

President: Dr. Harry W. Kaessler, 147 Prospect Ave., Mount Vernon, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.
Place: The Roger Smith Hotel, White Plains, N. Y. Time: Fourth Thursday of every other month from September to June (dinner meetings).

WICHITA PEDIATRIC SOCIETY

President: Dr. Walter L. Schafer, 401 N. Emporia St., Wichita 2, Kan.
Secretary: Dr. William F. McGuire, 401 N. Emporia St., Wichita 2, Kan.
Place: Variable. Time: First Thursday of each month.

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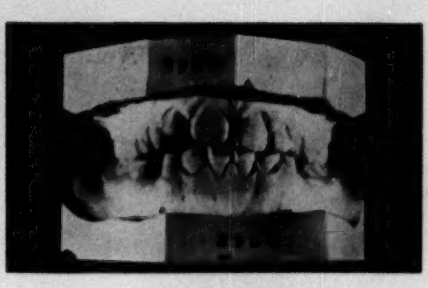

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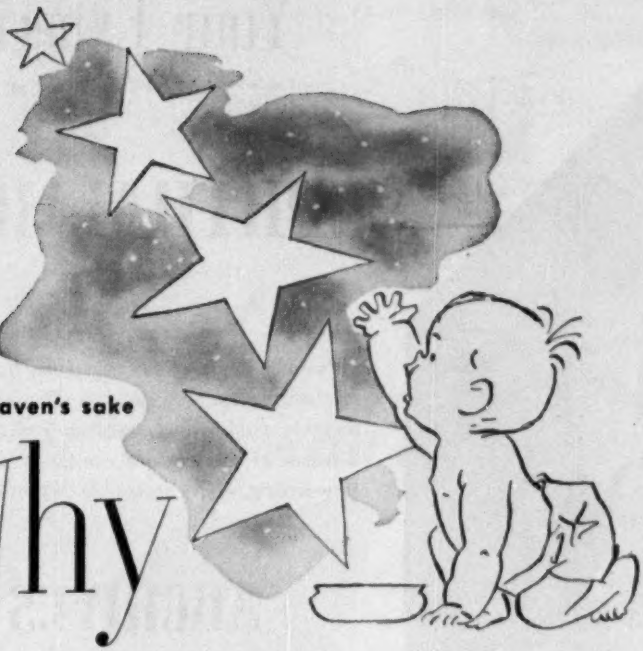

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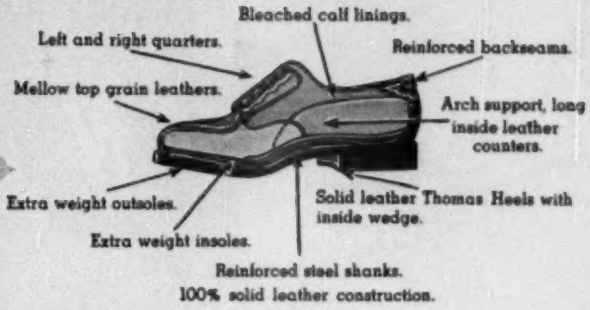

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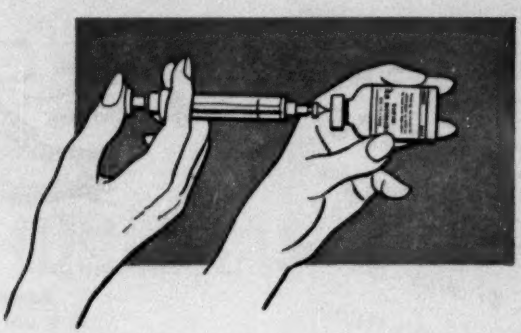

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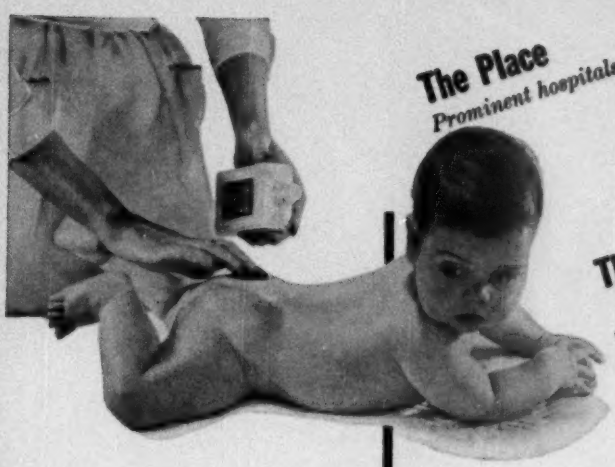

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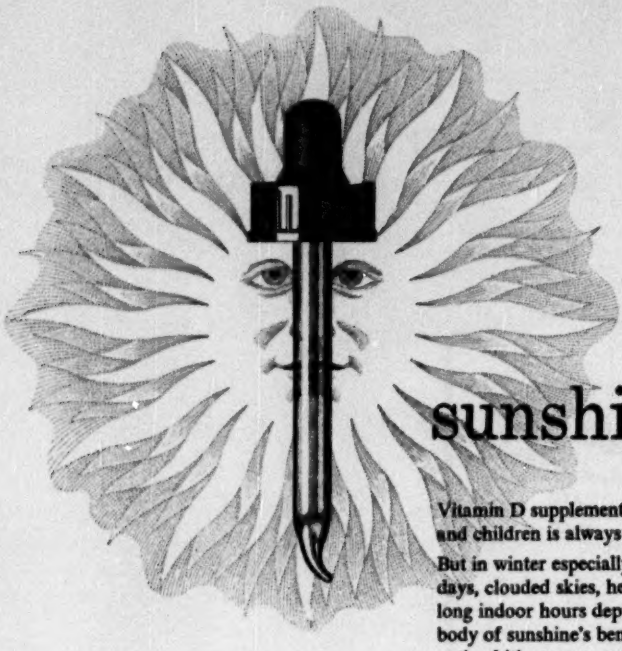

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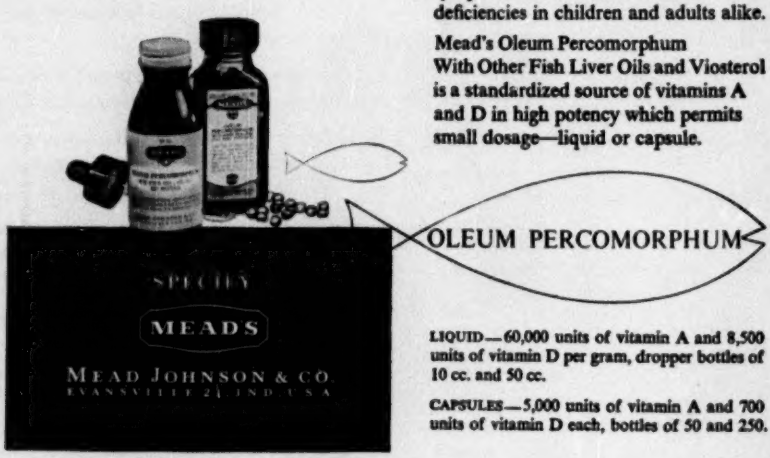

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